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(71) Applicant *(for all designated States except US)*: **PANACEA BIOTEC LIMITED** [IN/IN]; B-1 Extn./A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110044 (IN).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **JAIN, Rajesh** [IN/IN]; B-1 Extn./A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110044 (IN). **SINGH, Sukhjeet** [IN/IN]; B-1 Extn./A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110044 (IN). **DEVARAJAN, Sampath Kumar** [IN/IN]; B-1 Extn./A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110044 (IN).

(74) Agent: **GUPTA, Bhartee**; B-1 Extn./A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110044 (IN).

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Declarations under Rule 4.17:
— *as to the identity of the inventor (Rule 4.17(i))*

[Continued on next page]

(54) Title: INJECTABLE COMPOSITIONS, PROCESSES AND USES THEREOF

Figure 4

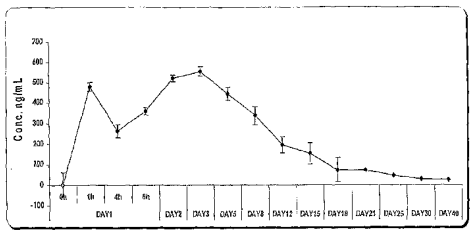
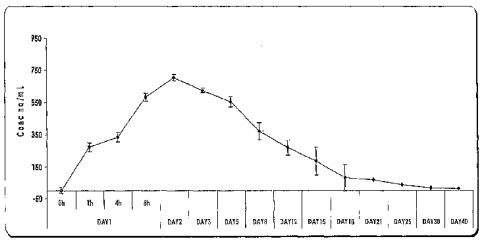


Figure 5



(57) Abstract: Injectable depot gel or implant compositions comprising at least one active agent(s) selected from a group comprising antipsychotics, aromatase inhibitors, alpha-1 adrenergic blocking agents, acetylcholinesterase inhibitors, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more pharmaceutically acceptable excipient(s) are provided. The present invention also describes process for preparation of such compositions and method of using such compositions.

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INJECTABLE COMPOSITIONS, PROCESSES AND USES THEREOF

FIELD OF THE INVENTION

The present invention describes single-component or a multi-component injectable compositions comprising at least one active agent(s) selected from a group comprising antipsychotics, aromatase inhibitors, alpha-1 adrenergic blocking agents, acetylcholinesterase inhibitors or pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and one or more pharmaceutically acceptable excipient(s), such that the said composition is in the form of ready-to-use liquid solution or dispersion, or a reconstitutable composition. The injectable compositions of the present invention preferably form a depot upon administration in vivo and are in the form of an in situ gelling composition or an implant composition which provides a prolonged release of the active agent(s) for extended periods of time. Particularly the present invention relates to injectable depot compositions comprising as the active agent at least one antipsychotic preferably ziprasidone or olanzapine or aripiprazole, or at least one aromatase inhibitor preferably anastrozole or letrozole, or at least one adrenergic blocking agent preferably tamsulosin, or at least one acetylcholinesterase inhibitor preferably donepezil. The present invention also describes process for preparation of the compositions and method of using such compositions. The compositions of the present invention increase the efficacy of treatment associated with particularly chronic diseases, leading to greater patient compliance.

BACKGROUND OF THE INVENTION

It is often desirable to administer drugs using controlled or sustained release formulations that can maintain therapeutic blood levels of the active agent (drug) over extended periods of time. These controlled release formulations reduce the frequency of dosing for enhanced patient convenience and compliance, and also reduce the severity and frequency of associated side effects. By maintaining substantially constant blood levels and avoiding blood level fluctuations of the drug particularly associated with conventional immediate release formulations that are administered several times a day, controlled or sustained release formulations can provide a better therapeutic profile

than is obtainable with conventional immediate release formulations. It is also often desirable to extend the release time of an injected drug to increase its duration of action, or to reduce its toxic effects. Formulations that are readily soluble in the body are usually absorbed rapidly and provide a sudden burst of available drug as opposed to a more desirable and gradual release of the pharmacologically active agent. This 'burst' release often results in a substantial portion of the beneficial agent, if not all, being released in a very short time, e.g., hours or 1-2 days. Several attempts have been made to provide controlled release injectable pharmaceutical compositions, but have not succeeded in overcoming certain problems associated with long acting parenteral dosage forms, such as achieving an extended release over desired period, stability in tissue fluids, reduced toxicity, reproducibility in preparations, and undesired physical, biochemical, or toxicological effects associated with dosage form compositions.

Where patient compliance is an issue, a probable approach is to design long acting dosage form compositions of the medication, that is, dosage forms where a single administration leads to a sustained release of the medication over an extended period of time. More recently formulations have been developed which are injected as a liquid, but undergo a change to a solid formulation in vivo, so-called 'in situ gelling systems'. These formulations can be injected intramuscularly or subcutaneously through small bore needles and employ in particular biocompatible, solvents. Further, these 'in situ gelling systems' are patient compliant and they simplify the dosage regimen that a patient needs to adhere to, thus reducing the opportunity for non-compliance that occurs with a more rigorous schedule of frequent administration. Among such dosage forms is the depot formulation, which can be administered in various ways including intramuscularly or subcutaneously by injection. The depot injection is specifically formulated to provide a sustained release of the medication over an extended period of time like days, weeks, months or even up to years. Other method employed is the use of an implant which is a device which is either expelled from the animal once administration has completed or the implant breaks down in the animal and is expelled during normal bodily functions.

The use of injectable implants for the delivery of drugs is well known. Both biodegradeable and non-biodegradeable implant versions have been marketed since the 1980s. Examples of these are Zoladex®, a polylactide-co-glycolide formulation of

goserelin for the treatment of breast cancer and Norplant®, a non-biodegradeable silicone device for contraception. Small, injectable microparticle based formulations are also well known, an example being Lupron Depot®, a formulation of leuprolide for the treatment of prostate cancer. A drawback of such preformed delivery systems is administration. Cylindrical rods such as Zoladex® require relatively large bore needles for implantation. However, injectable formulations comprising microparticles or nanoparticles allow smaller bore needles to be used for in vivo administration. The formulations are preferably in the form of microparticles which are difficult and highly cumbersome to formulate, and also require specialized manufacturing equipments and facilities. More recently formulations have been developed which are injected as a liquid, but undergo a change to a solid formulation in vivo, which are referred to as "in situ gelling systems".

Ziprasidone is a psychotropic agent which is indicated for treatment of schizophrenia. It is also known to possess moderate anti-depressant effects. Ziprasidone is available as GEODON® capsules containing monohydrochloride, monohydrate salt of ziprasidone in 20 mg, 40 mg, 60 mg and 80 mg strengths. Olanzapine is a psychotropic agent useful in the treatment of schizophrenia, acute manic episodes in bipolar disorder, acute agitation associated with both these disorders, maintenance treatment in bipolar disorder and for the treatment of depressive episodes associated with bipolar disorder. It is available as ZYPREXA® tablets in 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, or 20 mg strengths; ZYPREXA® ZYDIS® orally disintegrating tablets in 5 mg, 10 mg, 15 mg, or 20 mg strengths and ZYPREXA® IM injection wherein each vial provides 10 mg of olanzapine. Aripiprazole is an atypical antipsychotic approved for the treatment of schizophrenia. Aripiprazole is commercially available as ABILIFY® tablets in 2mg, 5mg, 10mg, 15mg, 20mg, and 30mg strengths.

Aromatase inhibitors are a class of compounds that act systematically to inhibit oestrogen synthesis in tissues. These compounds prevent oestrogen biosynthesis by inhibiting the enzyme aromatase, which catalyses the conversion of adrenal androgens (androstenedione and testosterone) to oestrogens (oestrogen and oestradiol). There has therefore been interest in developing these compounds as potential therapies for hormone responsive breast cancer in post-menopausal women. Anastrozole is a non-steroidal aromatase inhibitor which is indicated for adjuvant treatment of

postmenopausal women with hormone receptor positive early breast cancer. Anastrozole is commercially available under the trade name ARIMIDEX® as 1 mg oral tablet. Letrozole is a nonsteroidal competitive inhibitor of the aromatase enzyme system; it inhibits the conversion of androgens to estrogens. Letrozole is commercially available under the trade name FEMARA® as 2.5 mg tablets for oral administration.

Tamsulosin is an alpha1-adrenoceptor blocking agent, which exhibits selectivity for alpha1-receptors in the human prostate. Tamsulosin is used for the treatment of the symptoms associated with benign prostatic hyperplasia, such as bladder outlet obstruction, which is comprised of static and dynamic components. Tamsulosin hydrochloride is available under the trade name FLOMAX™ capsule containing 0.4 mg of tamsulosin hydrochloride. Donepezil is a known reversible inhibitor of acetylcholinesterase useful in the treatment of a variety of disorders, including dementia and attention deficit disorder. In particular, donepezil hydrochloride is employed as a pharmaceutically active agent for the symptomatic treatment of mild to moderate Alzheimer's dementia and is currently formulated as film-coated tablets of 5 mg and 10 mg doses for once a day oral administration available as ARICEPT®.

US Publication No. 20020034532 discloses injectable depot gel composition comprising a biocompatible polymer; a solvent that dissolves the biocompatible polymer and forms a viscous gel; a beneficial agent; and an emulsifying agent in the form of a dispersed droplet phase in the viscous gel. US patent No. 6287588 claims a dual phase polymeric agent delivery composition comprising a continuous biodegradable hydrogel phase, a discontinuous particulate phase comprising defined microparticles; and an agent to be delivered contained in at least said discontinuous particulate phase. The bioactive agent release is described to be modulated by microparticle phase alone or in both the microparticle and the gel matrix. The invention describes a reverse thermal gelation type of matrix. But the invention does not describe the experimental proof of polymeric hydrogel formation at the injection site by non solvent effect by a using an unhydrated cellulosic polymer in the reconstituted suspension composition having easy syringibility to be used as a depot injection. US publication no. 20060154918 discloses an injectable nanoparticulate olanzapine composition comprising olanzapine nanoparticles having an effective average particle

size that results in a therapeutic efficacy of about one week or greater; at least one surface stabilizer; and a pharmaceutically acceptable carrier.

US publication no. 20050153841 discloses a formulation for parenteral administration to a subject, comprising at least one water miscible solvent; at least one gelling agent; and at least one active agent; characterized in that the gelling agent is in particulate form and suspended in the solvent. But the invention has not described the dual modulation of drug release patterns by means of simultaneously using gelling system dispersed with release controlling particulate form of drug in biodegradable microparticles. US publication no. 20040024069 describes an injectable depot composition comprising a bioerodible, biocompatible polymer; a solvent having a miscibility in water of less than or equal to 7% at 25°C, in an amount effective to plasticize the polymer and form a gel therewith, wherein said solvent is an aromatic alcohol; a thixotropic amount of a thixotropic agent mixed with the polymer solution effective to form a thixotropic composition, the thixotropic agent being selected from the group consisting essentially of lower alkanols and said amount being less than 15 weight percent of the combined weight of the solvent and the thixotropic agent; and a beneficial agent. US publication no. 20040138237 describes an injectable depot formulation that is viscous, or becomes viscous in situ, comprising a solubilised ziprasidone. The solubilised ziprasidone cyclodextrin lyophilized complex is suspended in non-aqueous viscosity agents like aluminum monostearate gelled sesame oil; and in situ gelling system such as e.g. stearic acid and N-methyl pyrrolidone.

PCT publication no. WO2007026145 describes a slow release anastrozole formulation, more particularly an in-situ gelling formulation comprising a polylactide polymer or poly(lactide-co-glycolide) co-polymer, in which anastrozole is incorporated. PCT publication no. WO2007026138 describes a slow release anastrozole formulation, more particularly to biodegradable polymers, typically a polylactide or poly(lactide-co-glycolide) co-polymer, in which anastrozole is incorporated, including microparticle formulations and monolithic implant formulations. US patent no. 5,278,201 describes a biodegradable polymer for use in providing syringeable, in-situ forming, solid biodegradable implants for animals.

Several attempts to provide dosage form compositions to sustain medication levels including the use of biodegradable materials for delivery of active agent for extended periods of time have been described previously. Many sustained release parenteral compositions can exhibit an increased release of biologically active agent over the first twenty-four hours after administration, commonly referred to as a burst. In some instances, this burst can result in an undesirable increase in the levels of biologically active agent leading to toxic effects and/or minimal release of agent thereafter providing sub-therapeutic concentration of the active agent. Therefore, a need still exists for methods of preparing sustained release parenteral depot composition where additional control over release kinetics by, for example, reducing the burst release of the active agent can be exerted and a continuous release of active agents for longer period of duration, for example, for a week or a month or for 3 months or more can be achieved, yet possessing good syringibility characteristics.

Further, the prolonged release compositions comprising biodegradable polymers needs to be delivered inside the body. In such cases, the drug is incorporated into the polymer and the mixture shaped into a certain form such a cylinder, disc, or fiber for implantation. With such solid implants, the composition has to be inserted into the body through an incision. These incisions are often larger than desired by the medical profession and lead to a reluctance of the patients to accept such an implant or drug delivery system. The only way to avoid the incision with these polymers is to inject them as small particles, microspheres, or microcapsules. Although these small particles can be injected into the body with a syringe, they do not always satisfy the demand for a uniform in-situ depot gel or a biodegradable implant. Because they are particles, they do not form a continuous film or solid implant with the structural integrity upon injection into the body. When these small particles, microspheres, or microcapsules come in contact with the bodily fluids, these are poorly retained because of their small size and discontinuous nature. In addition, microspheres or microcapsules prepared from these polymers and containing drugs for release into the body are sometimes difficult or are expensive to produce on a large scale, and their storage and injection characteristics present problems.

Also, there is an unmet need for depot injectable compositions particularly for long-term use that are clinically tolerable, effective and safe, have a low potential for causing

morbidity, easy to manufacture, and are cost-effective. Such compositions would highly improve patient compliance since they would abolish the need for daily administration of the drug for substantially long duration of treatment. The present invention provides in situ gelling depot or implant compositions which alleviates the limitations of the prior art.

SUMMARY OF THE INVENTION

It is an objective of the present invention to provide injectable compositions comprising at least one active agent(s) selected from a group comprising antipsychotics, aromatase inhibitors, alpha-1 adrenergic blocking agents, acetylcholinesterase inhibitors and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein said compositions provide a prolonged release of the active agent(s) for extended periods of time.

It is an objective of the present invention to provide injectable compositions comprising as the active agent at least one antipsychotic preferably ziprasidone or olanzapine or aripiprazole, or at least one aromatase inhibitor preferably anastrozole or letrozole, or at least one adrenergic blocking agent preferably tamsulosin, or at least one acetylcholinesterase inhibitor preferably donepezil, or pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), which are in the form of an in situ gelling composition or an implant composition and which form a depot upon administration in vivo upon contact with body fluids thereby providing a prolonged release of the active agent for extended periods of time.

It is an objective of the present invention to provide a single-component or a multi-component injectable depot composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives,

isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof from about 0.1% w/w to about 95% w/w; at least one biocompatible bioerodible polymer(s) in an amount of from about 0.1% w/w to about 95% w/w; at least one biocompatible non-toxic solvent(s) in an amount of from about 0.1% w/w to about 95% w/w and one or more pharmaceutically acceptable excipient(s) in an amount of from about 0% to about 99.8% w/w based upon the total weight of the composition, such that the said composition is in the form of ready-to-use liquid solution or dispersion, or a reconstitutable composition, and such that the said composition provides a prolonged release of the active agent(s) for extended periods of time.

It is an objective of the present invention to provide a single-component composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more pharmaceutically acceptable excipient(s), wherein the said composition is in the form of ready-to-use solution or dispersion.

It is an objective of the present invention to provide a multi-component composition comprising of at least two components component-1 and component-2 such that the said composition is in the form of a reconstitutable composition, wherein component-1 comprises at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof, optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein component-2 for reconstitution of component-1 comprises at least one biocompatible non-toxic solvent(s), optionally at least one biocompatible bioerodible polymer(s) and optionally one or more excipient(s).

It is an objective of the present invention to provide injectable compositions comprising as the active agent at least one antipsychotic preferably ziprasidone or olanzapine or

aripiprazole, or at least one aromatase inhibitor preferably anastrozole or letrozole, or at least one adrenergic blocking agent preferably tamsulosin, or at least one acetylcholinesterase inhibitor preferably donepezil, or pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), and which is further diluted with an aqueous, hydro-alcoholic or oily liquid vehicle prior to parenteral administration.

It is an objective of the present invention to provide injectable compositions comprising at least one active agent selected from a group comprising ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the biocompatible bioerodible polymer(s) is a lactic or glycolic acid based polymer preferably polylactide polymer (PLA), or a polyglycolide polymer, or a poly(lactide-co-glycolide) co-polymer (PLGA); and wherein the said composition forms a gel or implant when placed in an aqueous physiological-type environment and releases the active agent for over a period of at least 3 days.

It is an objective of the present invention to provide a single-component or a multi-component injectable depot composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more pharmaceutically acceptable excipient(s), wherein the composition additionally comprises at least one gelling agent(s) preferably in an unhydrated form.

It is an objective of the present invention to provide a single-component or a multi-component injectable depot composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole,

letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more pharmaceutically acceptable excipient(s), wherein the said biocompatible non-toxic solvent(s) is capable of dissolving or dispersing the active agent and the biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein upon administration in vivo the composition is capable of precipitating to form a substantially cohesive gel or implant almost instantaneously.

It is also an objective of the present invention to provide injectable depot compositions which provides a flowable composition for forming a solid or semi-solid biodegradable gel or implant in situ within a living body comprising ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil as active agent, at least one biocompatible bioerodible polymer(s) and at least one biocompatible non-toxic solvent(s), optionally at least one gelling agent(s) and optionally along with one or more pharmaceutically acceptable excipient(s), and wherein the composition upon in vivo administration exhibits minimal burst effect thus avoiding dose dumping and providing a sustained release of the active agent for a prolonged duration.

It is another objective of the present invention to provide a method of forming a depot gel or an implant in situ, in a living body, which comprises preparing an in situ gelling formulation according to the method described herein, placing the formulation within the body and allowing the liquid vehicle to disperse or dissipate to produce a solid or gel implant.

It is yet another objective of the present invention to provide a pharmaceutical kit suitable for in situ formation of a biodegradable depot gel or implant from the compositions as described herein, in the body of a subject in need thereof, which comprises a device containing ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil as active agent, optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutical acceptable excipient(s); and a device containing at least one biocompatible non-toxic

solvent(s), optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); wherein the devices allow for expulsion of the contents of the two devices for enabling mixing together prior to administration of the contents into the body of the subject in need thereof.

It is another objective of the present invention to provide process for preparation of such injectable compositions which comprises mixing together the active agent(s), at least one biocompatible bioerodible polymer(s), at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s) to form a single-component ready-to-use liquid solution or dispersion; or preparing a multi-component reconstitutable composition which comprises preparation of component-1 using the active agent(s) alone or mixing the active agent(s) together with at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s), and preparation of component-2 using at least one biocompatible non-toxic solvent(s) alone or a dispersion or solution thereof comprising at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s) dispersed or dissolved in the biocompatible non-toxic solvent(s), and reconstituting the component-1 using the component-2 prior to administration.

It is still another objective of the present invention to provide use of an in situ gelling formulation as described herein in the manufacture of a medicament for the treatment of a condition treatable by ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil in a mammal particularly a human being.

It is yet another objective of the present invention to provide a method of using the compositions of ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil according to the present invention which comprises administering to a subject/patient in need thereof an effective amount of the said composition.

Preferably the composition is administered to a subject particularly human or animal by injection, wherein the composition forms a drug depot that releases the pharmaceutically active agent(s) over a desired extended period of time, thereby

increasing the efficacy of treatment associated with particularly chronic diseases, leading to greater patient compliance.

The compositions of the present invention preferably provide the active agent(s) to localize substantially in certain tissues, thereby increasing the efficacy of treatment, associated with such tissues. The compositions of the present invention are useful for prophylaxis, amelioration and/or treatment of disease(s) or disorder(s) in a subject in need thereof.

DETAILED DESCRIPTION OF THE DRAWINGS

Figure 1: The said figure shows the in-vitro release profile of the composition as mentioned hereinafter in Example-1.

Figure 2: The said figure shows the in-vitro release profile of the composition as mentioned hereinafter in Example-2.

Figure 3: The said figure shows the in-vitro release profile of the composition as mentioned hereinafter in Example-3.

Figure 4: The said figure shows the plasma concentration vs. time of the composition (Letrozole Depot Injection, SC) as mentioned hereinafter in Example-7.

Figure 5: The said figure shows the plasma concentration vs. time of the composition (Letrozole Depot Injection, IM) as mentioned hereinafter in Example-7.

Figure 6: The said figure shows the in-vitro release profile of the composition as mentioned hereinafter in Example- 8.

Figure 7: The said figure shows the in-vitro release profile of the composition as mentioned hereinafter in Example- 9.

Figure 8: The said figure shows the plasma concentration vs. time of the composition (Tamsulosin Depot Injection, IM) as mentioned hereinafter in Example-9.

Figure 9: The said figure shows the plasma concentration vs. time of the composition (Tamsulosin SC) as mentioned hereinafter in Example-9.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides injectable compositions comprising at least one active agent(s) selected from a group comprising antipsychotics, aromatase inhibitors, alpha-1

adrenergic blocking agents, acetylcholinesterase inhibitors and their pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s). The said compositions provide a prolonged release of the active agent(s) for extended periods of time.

The term "biocompatible" in the context of the present invention means not causing substantial tissue irritation or necrosis at the depot gel or implant site. The term "bioerodible" in the context of the present invention means that the implant erodes or degrades at its surfaces over time due, at least in part, to contact with substances found in the surrounding tissue fluids, or by cellular action. The term "non-toxic" implies that the agent does not cause any substantially potential toxicity upon in vivo use.

One of the biggest challenges in the development of solvent based depot injections in which the polymer is either dissolved or dispersed in a suitable solvent system is to overcome the development of high viscosity in the injectable compositions. Such systems as a result of high viscosity are difficult to withdraw into the syringe as well as cause painful administration to the patient. Such compositions also cannot be filtered via simple technique such as membrane filtration. Thus the appropriate selection of a solvent system poses difficulties to the formulation scientist. It has now been surprisingly found by the inventors of the present invention that the solvents as disclosed in context of the present invention improve the syringibility by having a low viscosity. This decrease in viscosity leads to improved syringibility and requires only membrane filtration step for sterilization thereby preventing the need for costly sterilization techniques such as gamma-radiation. Thus, patient compliance is enhanced which is paramount owing to low viscosity of the in-situ gelling composition in the instant invention as pain at injection site is considerably reduced compared to a conventional high viscosity injectable composition.

In an embodiment, the present invention provides injectable compositions comprising as the active agent at least one antipsychotic preferably ziprasidone or olanzapine or aripiprazole, or at least one aromatase inhibitor preferably anastrozole or letrozole, or at

least one adrenergic blocking agent preferably tamsulosin, or at least one acetylcholinesterase inhibitor preferably donepezil; or pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), which are in the form of an in situ gelling composition or an implant composition and which form a depot upon administration in vivo upon contact with body fluids therefore providing a prolonged release of the active agent for extended periods of time. The active agent 'ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil' wherever disclosed in the entire description of the present invention also encompasses its pharmaceutically acceptable salts, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms, derivatives or mixtures thereof.

The injectable compositions of the present invention aid in patient compliance as the compositions of the present invention provide the desired therapeutic plasma concentrations for optimum therapeutic benefit by abolishing the need to administer a dosage composition daily, which the present invention provides in the form of injectable compositions. The injectable compositions of the present invention leads to less frequent dosing of drugs, and still provides an improved therapeutic effect with reduced side effects by effectively smoothening out the fluctuations in the plasma concentration-time profile. Most importantly, the prolonged release formulations of the present invention improves the "quality of life" of patients undertaking treatment with ziprasidone or olanzapine or aripiprazole for schizophrenia, anastrozole or letrozole for oncology indications, tamsulosin for Benign Prostatic Hyperplasia (BPH) particularly seen in older individuals, and donepezil for dementia associated with Alzheimer's disease and/or attention deficit disorder.

In an embodiment, the present invention provides injectable compositions comprising as the active agent at least one antipsychotic preferably ziprasidone or olanzapine or aripiprazole, or at least one aromatase inhibitor preferably anastrozole or letrozole, or at least one adrenergic blocking agent preferably tamsulosin, or at least one acetylcholinesterase inhibitor preferably donepezil, or pharmaceutically acceptable

salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), which are in the form of an in situ gelling composition or an implant composition and which form a depot upon administration in vivo upon contact with body fluids thereby providing a prolonged release of the active agent for extended periods of time.

The amount of the active agent incorporated into the injectable, in-situ, solid forming implant depends upon the desired release profile, the concentration of drug required for a biological effect, and the length of time that the drug has to be released for treatment. There is no critical upper limit on the amount of drug incorporated into the polymer solution except for that of an acceptable solution or dispersion viscosity for injection through a syringe needle. The lower limit of drug incorporated into the delivery system is dependent simply upon the activity of the drug and the length of time needed for treatment. For the purposes of this specification 'depot' is defined as a substance (preferably containing an active agent) that is retained in close proximity to the site of injection so that release of the active agent occurs over a prolonged period of time. In an embodiment, the depot erodes/dissolves in the in vivo environment of a subject over time and in doing so releases the active agent into the subject.

In a preferred embodiment of the present invention is provided a single-component or a multi-component injectable depot composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof from about 0.1% w/w to about 95% w/w; at least one biocompatible bioerodible polymer(s) in an amount of from about 0.1% w/w to about 95% w/w; at least one biocompatible non-toxic solvent(s) in an amount of from about 0.1% w/w to about 95% w/w and one or more pharmaceutically acceptable excipient(s) in an amount of from about 0% to about 99.8% w/w based upon the total weight of the composition, such that the said composition is in the form of ready-to-use liquid solution or dispersion, or a reconstitutable composition, and such that the said composition

provides a prolonged release of the active agent(s) for extended periods of time. The compositions are in the form of a clear solution or a homogeneous dispersion that are capable of forming a depot upon administration in vivo upon contact with body fluids therefore providing a prolonged release of the active agent for extended periods of time.

In an embodiment, the present invention provides a single-component composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more excipient(s), wherein the said composition is in the form of ready-to-use liquid solution or dispersion.

In another embodiment, the present invention provides a multi-component composition comprising of at least two components component-1 and component-2 such that the said composition is in the form of a reconstitutable composition, wherein component-1 comprises at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof, optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein component-2 for reconstitution of component-1 comprises at least one biocompatible non-toxic solvent(s), optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s).

The compositions of the present invention are capable of producing a prolonged release of the active agents for at least 3 days preferably for a period of at least 7-15 days to 6 months or more. In another preferred embodiment, the biocompatible bioerodible polymer(s) is a lactic or glycolic acid based polymer preferably polylactide polymer (PLA), or a polyglycolide polymer, or a poly(lactide-co-glycolide) co-polymer (PLGA).

The present invention provides injectable depot compositions comprising ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil as active agent which are flowable and which are capable of forming a solid or semi-solid biodegradable gel or implant in situ within a body. In another embodiment, the present invention provides an in situ gelling composition comprising the active agent and preferably a PLGA polymer, dissolved or dispersed or suspended in suitable solvent optionally further dissolved or dispersed or suspended in a liquid diluent such as an aqueous vehicle or an organic solvent or an oily vehicle. The compositions of the invention, upon contact with water or bodily fluids, result in the precipitation of both the polymer and the active agent and subsequent formation of a gel or an implant within which the active agent is incorporated. The active agent(s) subsequently diffuse from the gel or implant over an extended period of time to provide the desired pharmacological effect.

The term "flowable" in context of present invention means having a viscosity that will permit displacement of a material having this characteristic without application of pressure. A flowable composition is manipulatable, will pass through a small/moderate sized orifice without application of pressure and may be shaped/molded within tissue defect. Flowable compositions in this context include those having a consistency from that of an emulsion or suspension with a low viscosity or water-like consistency, to that of a high viscosity such as cold molasses.

In an embodiment, the single-component or a multi-component injectable depot composition of the present invention comprises at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more pharmaceutically acceptable excipient(s), wherein the said biocompatible non-toxic solvent(s) is capable of dissolving or dispersing the active agent and the biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein upon administration in vivo the composition is capable of precipitating to form a substantially cohesive gel or implant almost instantaneously.

In another embodiment, the injectable depot compositions of the present invention provide a flowable composition for forming a solid or semi-solid biodegradable gel or implant in situ within a living body comprising ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil as active agent, at least one biocompatible bioerodible polymer(s) and at least one biocompatible non-toxic solvent(s), optionally at least one gelling agent(s) and optionally along with one or more pharmaceutically acceptable excipient(s), wherein the composition upon in vivo administration exhibits minimal burst effect thus avoiding dose dumping and providing a sustained release of the active agent for a prolonged duration.

In a further embodiment of the present invention is provided a single-component or a multi-component injectable depot composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more pharmaceutically acceptable excipient(s), wherein the composition additionally comprises at least one gelling agent(s) preferably in an unhydrated form.

In another embodiment, the present invention provides injectable compositions comprising at least one active agent selected from a group comprising ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s) in the form of a multi-component system preferably comprising at least two components.

In accordance with an aspect of the present invention is provided a two-component composition comprising of component-1 and component-2 such that the said composition is in the form of a reconstitutable composition, wherein component-1 comprises at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and

pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof, optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein component-2 for reconstitution of component-1 comprises at least one biocompatible non-toxic solvent(s), optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein the composition optionally comprise at least one gelling agent(s) either present in component-1 or component-2 or both. The gelling agent(s) is present in an unhydrated form. In another embodiment, the gelling agent(s) is a biocompatible cellulosic polymer which acts as a stabilizer, active agent release modifier and/or a gel forming agent.

In an embodiment of the present invention, the gelling agent is selected from but not limited to group comprising cellulose derivatives, such as hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropyl methyl cellulose, methylcellulose, sodium carboxymethyl cellulose and its derivatives, vinyl polymers, polyoxyethylene-polyoxypropylene polymers or co-polymers (Pluronics®) such as PEO_{99}-PPO_{67}-PEO_{99} known as Pluronics F127, polysaccharides such as glycosaminoglycans, agar, pectin, alginic acid, sodium alginate dextran, starch and chitosan, proteins, poly(ethyleneoxide), acrylamide polymers, polyhydroxy acids, polyanhydrides, polyorthoesters, polyamides, polycarbonates, polyalkylenes, polyalkylene glycols, polyalkylene oxides, polyalkylene terepthalates, polyvinyl alcohols such as polyacrylic acid, polymethacrylic acid, polyvinyl pyrrolidone and polyvinyl alcohol, polyvinyl ethers, polyvinyl esters, polyvinyl halides, polyvinylpyrrolidone, polysiloxanes, polyvinyl acetates, polystyrene, polyurethanes, synthetic celluloses, polyacrylic acids, polybutyric acid, polyvaleric acid, poly(lactide-co-caprolactone), and copolymers, derivatives, and the like; or mixtures thereof. It is the applicant's understanding that the gelling agent forms a gel or semi-solid on dispersal of the solvent. For the purpose of this application, 'gel' is defined as a viscous or solid like material formed by the aid of a suitable gelling agent. Such gels have a moderate to high viscosity that is they do not pour freely. These gelling agents are preferred due to their pharmaceutical and physiological acceptability and ability to form gels of desirable viscosity for use in such depot formation. Preferably the gelling agent(s) is a high viscosity grade of sodium

carboxymethyl cellulose or methylcellulose. Preferably gelling agent is present in an amount between about 0.1 to about 50%, more preferably between about 0.5 to about 50% by weight of either component-1 or component-2 or both.

In an embodiment, the present invention provides injectable compositions comprising at least one active agent selected from a group comprising ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the said biocompatible non-toxic solvent(s) is capable of dissolving or dispersing the active agent and/or the biocompatible bioerodible polymer(s); and wherein upon administration in vivo the composition is capable of precipitating to form a substantially cohesive gel or implant almost instantaneously.

In an embodiment of the present invention, the biocompatible bioerodible polymer is selected from but not limited to a group comprising lactic acid-based polymers such as polylactides e.g. poly (D,L-lactide) i.e. PLA; glycolic acid-based polymers such as polyglycolides (PGA) e.g. Lactel® from Durect; poly (D,L-lactide-co-glycolide) i.e. PLGA, (Resomer® RG-504, Resomer® RG-502, Resomer® RG-504H, Resomer® RG-502H, Resomer® RG-504S, Resomer® RG-502S, from Boehringer, Lactel® from Durect); polycaprolactones such as Poly(e-caprolactone) i.e. PCL (Lactel® from Durect); polyanhydrides; poly(Sebacic acid) SA; poly(Ricenolic acid) RA; poly(Fumaric acid), FA; poly(Fatty acid dimmer), FAD; poly(terephthalic acid), TA; poly(isophthalic acid), IPA; poly(p-{carboxyphenoxy}methane), CPM; poly(p-{carboxyphenoxy}propane), CPP; poly(p-{carboxyphenoxy}hexane), CPH; polyamines, polyurethanes, polyesteramides, polyorthoesters {CHDM: Cis/trans-cyclohexyl dimethanol, HD:1,6-hexanediol. DETOU: (3,9-diethylidene-2,4,8,10-tetraoxaspiro undecane)}; polydioxanones; polyhydroxybutyrates; polyalkyene oxalates; polyamides; polyesteramides; polyurethanes; polyacetals; polyketals; polycarbonates; polyorthocarbonates; polysiloxanes; polyphosphazenes; succinates; hyaluronic acid; poly(malic acid); poly(amino acids); polyhydroxyvalerates; polyalkylene succinates; polyvinylpyrrolidone; polystyrene; synthetic celluloses; polyacrylic acids; polybutyric acid; triblock copolymers (PLGA-PEG-PLGA), triblock

copolymers (PEG-PLGA-PEG), poly (N-isopropylacrylamide) (PNIPAAm), poly (ethylene oxide)- poly (propylene oxide)- poly (ethylene oxide) tri-block copolymers (PEO-PPO-PEO), polyvaleric acid; polyethylene glycol; polyhydroxycellulose; chitin; chitosan; polyorthoesters and copolymers, terpolymers; lipids such as cholesterol, lecithin; poly(glutamic acid-co-ethyl glutamate) and the like, or mixtures thereof.

Preferably the biodegradable polymer is a lactic acid-based polymer, more preferably polylactide, or poly (D, L-lactide-co-glycolide) i.e. PLGA. Preferably the biodegradable polymer is present in an amount between about 10% to about 98% w/w of the component-1. The lactic acid-based polymer has a monomer ratio of lactic acid to glycolic acid in the range of 100:0 to about 0:100 preferably 100:0 to about 10:90 and has an average molecular weight of from about 1,000 to 200,000 daltons. It might be emphasized that the choice and the quantity of biodegradable polymer is governed by the nature and quantity of active agent used, the desired particle size of the composition, the intended use, the duration of use, and the like. It might be emphasized that the choice and the quantity of biodegradable polymer is governed by the nature of active agent used, the intended use and the duration of use of the composition, and the like.

In an embodiment of the present invention, the biocompatible non-toxic solvent is selected from but not limited to a group comprising triacetin, ethanol, bezyl alcohol, 1-butanol, 2-butanol, chloroform, acetic acid, isopropyl alcohol, acetonitrile, N-methyl-2-pyrrolidone (NMP), 2-pyrrolidone, miglyol, glycerol, methyl acetate, methyl isobutyl ketone, benzyl benzoate, propylene glycol, dimethyl isosorbide, propylene carbonate, ethyl acetate, ethyl lactate, dimethyl sulfone, N,N-diethyl-m-toluamide, methyl ethyl ketone, dimethylformamide, dichloromethane, benzonitrile, dimethyl isosorbide, dimethyl sulfoxide, dimethyl acetamide, tetrahydrofuran, caprolactam, decymethylsulfoxide, oleic acid, and 1-dodecylazacyclo-heptan-2-one, and the like or mixtures thereof.

In an embodiment, the present invention provides injectable depot compositions comprising ziprasidone; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more excipient(s), wherein the solvent is selected from a group comprising N-methyl-2-pyrrolidone, dimethyl sulfoxide (DMSO), dimethyl formamide (DMF), methyl isobutyl ketone, or mixtures thereof.

In an embodiment, the present invention provides injectable depot compositions comprising olanzapine; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

In an embodiment, the present invention provides injectable depot compositions comprising aripiprazole; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

In an embodiment, the present invention provides injectable depot compositions comprising anastrozole; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

In an embodiment, the present invention provides injectable depot compositions comprising letrozole; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

In an embodiment, the present invention provides injectable depot compositions comprising tamsulosin; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide,

dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

In an embodiment, the present invention provides injectable depot compositions comprising donepezil; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

In another embodiment, the injectable compositions of the present invention comprising as the active agent at least one antipsychotic preferably ziprasidone or olanzapine or aripiprazole, or at least one aromatase inhibitor preferably anastrozole or letrozole, or at least one adrenergic blocking agent preferably tamsulosin, or at least one acetylcholinesterase inhibitor preferably donepezil, or pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), is further diluted with an aqueous, hydro-alcoholic or oily liquid vehicle prior to parenteral administration.

In a further embodiment of the present invention, the liquid vehicle is in the form of an aqueous vehicle comprising water and optionally water miscible solvent selected from but not limited to group comprising preferably a water-miscible alcohol, for example, ethanol, n-propyl alcohol, isopropyl alcohol, tert-butyl alcohol, ethylene glycol or propylene glycol; dimethylsulfoxide; decylmethylsulfoxide; dimethylformamide; N-methyl-2-pyrrolidone; 2-pyrrolidone; acetone; methyl acetate; ethyl acetate; caprolactam; oleic acid, and 1-dodecylazacycloheptan-2-one; a water-miscible ether, for example tetrahydrofuran; a water-miscible nitrile, for example acetonitrile; a water-miscible ketone, for example acetone or methyl ethyl ketone; an amide, for example dimethylacetamide; propylene glycol; glycerin, polyethylene glycol 400, glycofurol (tetraglycol), purified water and the like; or mixtures thereof. It is also preferred that the solvent for the biocompatible bioerodible polymer be non-toxic, water miscible, and otherwise biocompatible. Solvents that are toxic should not be used to inject any

material into a living body. The solvents must also be biocompatible so that they do not cause severe tissue irritation or necrosis at the site of implantation. Furthermore, the solvent should be water miscible so that it will diffuse quickly into the body fluids and allow water to permeate into the polymer solution and cause it to solidify. Preferably the solvent is selected from a group comprising glycerin, ethanol, propylene glycol, polyethylene glycols, NMP, and purified water.

The solubility of the biodegradable polymers in the various solvents will differ depending upon their crystallinity, their hydrophilicity, hydrogen-bonding, and molecular weight. Thus, not all of the biodegradable polymers will be soluble in the same solvent, but each polymer or copolymer should have its optimum solvent. Lower molecular-weight polymers will normally dissolve more readily in the solvents than high-molecular-weight polymers. As a result, the concentration of a polymer dissolved in the various solvents will differ depending upon type of polymer and its molecular weight. Conversely, the higher molecular-weight polymers will normally tend to solidify faster than the very low-molecular-weight polymers. Moreover the higher molecular-weight polymers will tend to give higher solution viscosities than the low-molecular-weight materials. Thus for optimum injection efficiency, the molecular weight and the concentration of the polymer in the solvent have to be controlled. For example, low-molecular-weight polylactic acid formed by the condensation of lactic acid will dissolve in N-methyl-2-pyrrolidone (NMP) to give a 73% by weight solution which still flows easily through a 23-gauge syringe needle, whereas a higher molecular-weight poly (DL-lactide) (DL-PLA) formed by the additional polymerization of DL-lactide gives the same solution viscosity when dissolved in NMP at only 50% by weight. The higher molecular-weight polymer solution solidifies immediately when placed into water. The low-molecular-weight polymer solution, although more concentrated, tends to solidify very slowly when placed into water.

In another embodiment of the present invention, the liquid diluent is a lipophilic or oily vehicle comprising at least one oily component selected from but not limited to a group comprising vegetable oils such as corn oil, sesame oil, coconut oil, almond oil, sunflower oil, castor oil, etc. or a lipophilic compound such as dimethyl isosorbide, optionally with a surfactant selected from a group comprising anionic, cationic, non-

ionic or zwitterionic surfactants and/or one or more other pharmaceutically acceptable excipient(s).

In another embodiment, the injectable depot compositions of the present invention comprise one or more pharmaceutically acceptable excipient(s) selected from but not limited to a group comprising one or more co-surfactants, solvents/co-solvents, water immiscible solvents, water, water miscible solvents, oily components, hydrophilic solvents, emulsifiers, preservatives, antioxidants, anti-foaming agents, stabilizers, buffering agents, pH adjusting agents, osmotic agents, channel forming agents, isotonicity producing agents, or any other excipient known to the art that is soluble or miscible or dispersible in the biocompatible non-toxic solvent(s), or mixtures thereof.

In an embodiment of the present invention, the co-surfactant is selected from but not limited to a group comprising polyethylene glycols; polyoxyethylene-polyoxypropylene block copolymers known as "poloxamer"; polyglycerin fatty acid esters such as decaglyceryl monolaurate and decaglyceryl monomyristate; sorbitan fatty acid ester such as sorbitan monostearate; polyoxyethylene sorbitan fatty acid ester such as polyoxyethylene sorbitan monooleate(TWEEN®); polyethylene glycol fatty acid ester such as polyoxyethylene monostearate; polyoxyethylene alkyl ether such as polyoxyethylene lauryl ether; polyoxyethylene castor oil and hardened castor oil, such as polyoxyethylene hardened castor oil; and the like or mixtures thereof. In an embodiment of the present invention, the solvent/cosolvent is selected from but not limited to a group comprising alcohols such as propylene glycol, polypropylene glycol, polyethylene glycol (such as PEG300, 400, 600, etc.), glycerol, ethanol, triacetin, dimethyl isosorbide, glycofurol, propylene carbonate, water, dimethyl acetamide, and the like or mixtures thereof. More preferably the solvent used is ethanol. The choice of solvent/cosolvent and its quantity primarily depends on solubility of active agent(s).

In an embodiment, the viscosity of the in-situ gelling composition is from about 1 cps to about 5000 cps. In another embodiment, the viscosity of the in-situ gelling composition is from about 1 cps to about 3000 cps. In yet another embodiment, the viscosity of the in-situ gelling composition is from about 1 cps to about 800 cps.

Suitable anti-foaming agents include for example silicon emulsions or sorbitan sesquioleate. Suitable stabilizers to prevent or reduce the deterioration of the other components in compositions of the present invention include antioxidants such as glycine, alpha-tocopherol or ascorbate, BHA, BHT, and the like or mixtures thereof. Suitable tonicity modifier includes for example mannitol, sodium chloride, and glucose. Suitable buffering agent includes for example acetates, phosphates, and citrates with suitable cations. It might be however understood that certain excipient(s) used in the present composition can serve more than one purpose.

In an embodiment, the present invention provides a method of forming a depot gel or an implant in situ, in a living body, which comprises preparing an in situ gelling formulation according to the method described herein, placing the formulation within the body and allowing the liquid vehicle to disperse or dissipate to produce a solid or gel implant.

In another embodiment, the present invention provides a pharmaceutical kit suitable for in situ formation of a biodegradable depot gel or implant from the compositions as described herein, in the body of a subject in need thereof, which comprises a device containing ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil as active agent, optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutical acceptable excipient(s); and a device containing at least one biocompatible non-toxic solvent(s), optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); wherein the devices allow for expulsion of the contents of the two devices for enabling mixing together prior to administration of the contents into the body of the subject in need thereof.

In an embodiment, the present composition comprises additionally a thermogelling or hydrogelling polymer, or the biocompatible bioerodible polymer according to the present invention is a temperature sensitive biocompatible polymer, for example, a block copolymer having thermal gelation properties wherein the polymer is a gel at physiological temperatures (about 37°C) and is a liquid above or below physiological temperatures would be functional. In the case of a gel having reverse thermal-gelation

properties, the block copolymer would be a liquid at temperatures below the gelation temperature and would form a gel at above the gelation temperature. Conversely, a block copolymer having conventional thermal-gelation properties would be a liquid above the gelation temperature and a gel at or below the gelation temperature. When a biocompatible block copolymer having reverse thermal-gelation properties is employed, the active agent can be loaded in the block copolymer at below physiological temperatures such as room temperature. Because such block copolymers are soluble in water when cooled, the active agent may be easily loaded within the solution. Furthermore, when administered, the block copolymer solution, once in the gel state, is able to retain the active agent.

In yet another embodiment, the in-situ gel responds reversibly to a change in one or more in vivo conditions such as temperature, pH, solvent and ionic conditions. Particularly, the in situ gel is able to imbibe or solubilize a large amount of therapeutic agent and deliver a substantially linear and sustained release of therapeutic agent under physiological conditions.

In yet another embodiment of the present invention is provided a process for preparation of such injectable compositions which comprises mixing together the active agent(s), at least one biocompatible bioerodible polymer(s), at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s) to form a single-component ready-to-use liquid solution or dispersion; or preparing a multi-component reconstitutable composition which comprises preparation of component-1 using the active agent(s) alone or mixing the active agent(s) together with at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s), and preparation of component-2 using at least one biocompatible non-toxic solvent(s) alone or a dispersion thereof comprising at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s) dispersed in the biocompatible non-toxic solvent(s), and reconstituting the component-1 using the component-2 prior to administration.

In an embodiment is provided a process for the preparation of injectable composition according to the present invention, which comprises of the following steps:

i) Dissolving or dispersing the active agent, biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s) in a biocompatible non-toxic solvent(s) and

ii) Filling the material of step (i) into a syringe suitable for parenteral administration.

In an embodiment is provided a process for the preparation of injectable composition according to the present invention, which comprises of the following steps:

i) Dissolving or dispersing the biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s) in a biocompatible non-toxic solvent(s),

ii) Lyophilizing and filling the active agent(s) optionally mixed with one or more pharmaceutically acceptable excipient(s) in a vial, and

iii) Reconstituting the material of step (ii) with the material of step (i) before administration.

In an embodiment is provided a process for the preparation of injectable composition according to the present invention, which comprises of the following steps:

i) Mixing the sterile active agent(s), biocompatible bioerodible polymer(s) and optionally one or more excipient(s),

ii) Filling the material of step (i) and the biocompatible non-toxic solvent(s) optionally comprising one or more pharmaceutically acceptable excipient(s) in separate chambers of pre-filled syringe, and

iii) Mixing the materials of the pre-filled syringe before administration.

In an embodiment is provided a process for the preparation of injectable composition according to the present invention, which comprises of the following steps:

i) Mixing the sterile active agent(s), biocompatible bioerodible polymer(s) and optionally one or more excipient(s),

ii) Filling the material of step (i) in a syringe,

iii) Filling the biocompatible non-toxic solvent(s) optionally comprising one or more pharmaceutically acceptable excipient(s) in a suitable container, and

iv) Reconstituting the material of step (ii) using the material of step (iii) before administration.

In another embodiment of the present invention is provided process for preparation of such composition which comprises of the following steps:

i) Dissolving or dispersing the active agent(s), biocompatible bioerodible polymer(s) and optionally one or more excipient(s) in biocompatible non-toxic solvent(s),

ii) Optionally making a liquid diluent composition (vehicle) comprising mixing a water miscible or immiscible solvent or an oily compound optionally with gelling agent(s) and/or other excipient(s), and

iii) Optionally reconstituting the material of step (i) with the material of step (ii) before administration.

In an embodiment of the present invention is provided process for preparation of such composition which comprises of the following steps:

i) Mixing the sterile active agent(s) with biocompatible bioerodible polymer(s),

ii) Mixing the material of step (i) optionally with gelling agent and/or optionally with one or more excipient(s),

iii) Dispersing material of step (ii) in a biocompatible non-toxic solvent(s) to form component-1,

iv) Mixing the liquid diluent (vehicle) optionally with gelling agent(s) and/or other excipient(s) to form component- 2, and

v) Mixing the component-1 and component-2 to obtain the desired composition before administration.

In an embodiment, the composition of the present invention is preferably in the form of parenteral composition which can be administered to a subject, animals or humans, preferably via intramuscular, intradermal, cutaneous or subcutaneous routes. Specifically the parenteral composition according to the present invention can be administered by any of the following routes such as among others: intra-abdominal, intra-articular, intra-capsular, intra-cervical, intra-cranial, intra-ductal, intra-dural, intra-lesional, intra-ocular, intra-locular, intra-mural, intra-operative, intra-parietal, intra-peritoneal, intra-plural, intra-pulmonary, intra-spinal, intra-thoracic, intra-tracheal, intra-tyrnpanic, intra-uterine or transdermal. In a preferred embodiment, the composition of the present invention is in the form of parenteral composition, which

may be administered via intramuscular or subcutaneous route.

In an embodiment, the in-situ gelling composition according to the present invention can deliver the active agent directly to the target and provide short or long-term treatment by the sustained release of the active agent in the target area. The depot formed in vivo upon injection of the compositions according to the present invention is of a consistency selected from the group consisting of a viscous material, a gel or semi-solid, and combinations thereof. The rate of release of the active agent from the depot might vary based on variation in one or more factors such as initial particle size, levels of gel in the formulation, the amount of active agent, levels of any additional materials in the formulation, the subject, subject metabolism, the administration site, and combinations thereof. A further advantage of the present invention is that leakage from the injection site is minimized or removed altogether. The biocompatible bioerodible polymer(s) that precipitates out upon contact with in vivo fluids instantaneously entraps substantially the active agent within close proximity of the injection site. This avoids back flow of formulation out through the injection point thus stopping unwanted waste of the agent and also gives a clean wound/administration area. In addition, the incorporation of a gelling agent into the composition of the present invention provides a better entrapment of the active agent and a lesser initial burst release of active agent after injection.

In yet another embodiment of the present invention is provided a method of forming a depot gel or an implant in situ, in a living body, which comprises preparing an in situ gelling formulation according to the method described herein, placing the formulation within the body and allowing the liquid vehicle to disperse or dissipate to produce a solid or gel implant.

In still another embodiment of the present invention is provided use of an in situ gelling formulation as described herein in the manufacture of a medicament for the treatment of a condition treatable by ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil in a mammal particularly a human being.

It is yet another objective of the present invention to provide a method of using the

compositions of ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil according to the present invention which comprises administering to a subject/patient in need thereof an effective amount of the said composition. For example, the compositions of the present invention comprising ziprasidone are particularly useful for management such as prophylaxis, amelioration and/or treatment of subjects for the signs and symptoms of schizophrenia; compositions comprising olanzapine are particularly useful for management such as prophylaxis, amelioration and/or treatment of schizophrenia, acute manic episodes in bipolar disorder, acute agitation associated with both these disorders, maintenance treatment in bipolar disorder and depressive episodes associated with bipolar disorder; compositions comprising aripiprazole are particularly useful for management such as prophylaxis, amelioration and/or treatment of schizophrenia; compositions comprising anastrozole are particularly useful for management such as prophylaxis, amelioration and/or treatment of postmenopausal women with hormone receptor positive early breast cancer; compositions comprising letrozole are particularly useful for the management such as prophylaxis, amelioration and/or treatment of hormonally-responsive breast cancer; compositions comprising tamsulosin are particularly useful for management such as prophylaxis, amelioration and/or treatment of subjects for the signs and symptoms of benign prostatic hyperplasia; and compositions comprising donepezil are particularly useful for the management such as prophylaxis, amelioration and/or treatment of mild to moderate Alzheimer's dementia and attention deficit disorder.

In still another embodiment is provided use of the composition according to the present invention comprising ziprasidone or olanzapine or aripiprazole as the active agent for the manufacture of a medicament for the prophylaxis, amelioration and/or treatment of signs and symptoms of schizophrenia. In another embodiment is provided the use of a composition according to the present invention comprising anastrozole or letrozole for the manufacture of a medicament for the prophylaxis, amelioration and/or treatment of subjects for oncology indications. In an embodiment is provided the use of a composition according to the present invention comprising tamsulosin for the manufacture of a medicament for the prophylaxis, amelioration and/or treatment of subjects for Benign Prostatic Hyperplasia (BPH). In another embodiment is provided the use of a composition according to the present invention comprising donepezil for the manufacture of a medicament for the prophylaxis, amelioration and/or treatment of

subjects for mild to moderate Alzheimer's dementia and attention deficit disorder.

Preferably the composition is administered to a subject particularly human or animal by injection, wherein the composition forms a drug depot that releases the pharmaceutically active agent(s) over a desired extended period of time, thereby increasing the efficacy of treatment associated with particularly chronic diseases, leading to greater patient compliance. The compositions of the present invention preferably provide the active agent(s) to localize in certain tissues, thereby increasing the efficacy of treatment, associated with such tissues. The compositions of the present invention are useful for prophylaxis, amelioration or treatment of disease(s) or disorder(s) in a subject in need thereof.

In an embodiment of the present invention, the compositions as mentioned hereinafter in Example-7 were subjected to bioavailability study conducted in healthy female rats. The protocol of the study is as follows:

Objective: The in-vivo pharmacokinetic profile of the above mentioned depot formulation in female rats via subcutaneous (SC) and intramuscular (IM) routes.

The selected rats of respective groups were administered depot formulation of letrozole subcutaneously and intramuscularly with 24/26 gauge needle and letrozole suspension per orally.

The in-vivo study for composition as mentioned hereinbefore was plotted as plasma concentration vs. time, the result of which is as follows:

S.No.	Time (days)	Mean Conc. (ng/ml) (Letrozole Depot Injection, IM)
1.	0.041	478.75
2.	0.16	261.75
3.	0.33	358.25
4.	2	521.5

5.	3	556
6.	5	444.25
7.	8	336.75
8.	12	195.55
9.	15	151.75
10.	18	71.17
11.	21	70.57
12.	25	45.55
13.	30	27.7
14.	40	25.95

S.No.	Time (days)	Mean Conc. (ng/ml) (Letrozole Depot Injection, SC)
1.	0.041	272.25
2.	0.16	334
3.	0.33	581
4.	2	704.25
5.	3	623.5
6.	5	553
7.	8	369.75
8.	12	268.3
9.	15	184.35
10.	18	78.32
11.	21	67.55
12.	25	36.15
13.	30	15.62
14.	40	9.39

In an another embodiment of the present invention, the compositions as mentioned hereinafter in Example 9 were subjected to bioavailability study conducted in New Zealand male rabbits (1.5-2.0 kg). The protocol of the study is as follows:

Objective: The in-vivo pharmacokinetic profile of the above mentioned depot formulation in male rabbits.

The above mentioned formulation was injected to animal and plasma concentration of the drug was detected in the animals. The following table represents the plasma concentration of the drug in animals at various time intervals.

S.No.	Time (Days)	Mean Conc. (ng/ml) (Tamsulosin IM)
1.	0.02	148.8
2.	0.041	139.77
3.	0.083	64.25
4.	0.16	29.35
5.	0.33	22.57
6.	2	15.45
7.	3	25.75
8.	4	29.77
9.	5	26.05
10.	6	21
11.	7	14.25
12.	10	3.99
13.	12	5.34
14.	15	3.83
15.	18	7.24
16.	21	4.81
17.	25	0.65
18.	30	0.10
19.	35	0
20.	40	0

S.No.	Time (Days)	Mean Conc. (ng/ml) (Tamsulosin SC)
1.	0.02	267.5

2.	0.041	314.75
3.	0.083	254.25
4.	0.16	111.9
5.	0.33	28.37
6.	2	12.65
7.	3	14.025
8.	4	16.057
9.	5	12.71
10.	6	6.74
11.	7	4.35
12.	10	2.87
13.	12	2.09
14.	15	2.19
15.	18	7.09
16.	21	5.80
17.	25	0.73
18.	30	0.05
19.	35	0
20.	40	0

In yet another embodiment of the present invention, the compositions as mentioned hereinafter in Example-10 were subjected to bioavailability study conducted in male rats (250 g). The protocol of the study is as follows:

Objective: The in-vivo pharmacokinetic profile of the above mentioned depot formulation in male rat.

The above mentioned formulation was injected to animal and plasma concentration of the drug was detected in the animals. The following table represents the plasma concentration of the drug in animals at various time intervals.

S.No.	Time (Days)	Mean Conc. (ng/ml) (Donepezil)
1.	0	0

2.	0.02	179.2
3.	0.041	263.5
4.	0.083	270.75
5.	0.16	259
6.	0.33	242
7.	1	34.7
8.	2	29.9
9.	3	22.19
10.	4	5
11.	6	2.01
12.	7	2.75
13.	9	10.28
14.	11	13.54
15.	14	14.52
16.	17	14.57
17.	21	11.33
18.	25	6.96
19.	30	3.07
20.	35	3.52
21.	40	2.69
22.	50	1.21
23.	60	1.06

The above-described exemplary embodiments are intended to be illustrative in all respects, rather than restrictive, of the present invention. Thus the present invention is capable of many variations in detailed implementation that can be derived from the description contained herein by a person skilled in the art. All such variations and modifications are considered to be within the scope and spirit of the present invention.

The examples given below serve to illustrate embodiments of the present invention. However they do not intend to limit the scope of the present invention.

Various experiments have been carried out on the present invention in order to ascertain the desirable viscosity of the injectable compositions which provide efficient syringibility of the injectables. This was done by selecting varied solvents selected from dimethylacetamide, dimethylisosorbide and N-methyl-2-pyrrolidone and different grades of polymers selected from PLGA 50/50 (low viscosity); PLGA 50/50 (high viscosity); PLGA 75/25 (low viscosity) and PLGA 75/25 (high viscosity) and their respective correlation amongst each other with respect to their impact on the final viscosity of the composition. It was concluded that the solvent dimethylacetamide along with polymer PLGA 50/50 (low viscosity) provided the most desirable viscosity, thus enhancing the syringibility of the injectable compositions.

A comparative data is represented as herein below which correlates the polymer with the solvent and thus substantiates the effective viscosity suitable for injectable compositions.

Polymer	**Weight (mg)**							
PLGA 50/50 (low viscosity)	-	-	225	75	-	-	-	-
PLGA 50/50 (high viscosity)	-	-	-	-	125	125	125	-
PLGA 75/25 (low viscosity)	-	-	-	-	-	-	-	225
PLGA 75/25 (high viscosity)	150	125	-	-	-	-	-	-
Solvent								
Dimethylacetamide	375	400	400	350	250	350	-	-
Dimethylisosorbide	-	-	-	-	100	-	-	-
N-methyl-2-pyrrolidone	-	-	-	-	-	-	350	275
Viscosity (cps)	**2781**	**617**	**123**	**186**	**687**	**325**	**841**	**925**

EXAMPLES

Example-1: Anastrozole depot injection

S. No.	**Ingredient**	**Quantity (g)/5 g**
1.	Anastrozole	0.3
2.	Poly (DL-lactide-co-glycolide) 50/50	1.2
3.	N, N Dimethyl Acetamide (DMA)	3.5

Procedure:

i) Anastrazole was weighed and dissolved in the required amount of DMA.

ii) Poly (DL-lactide-co-glycolide) (50/50) was added in the solution of step (i) after dissolving anastrazole in DMA.

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Example-2: Anastrozole depot injection

S. No.	Ingredient	Quantity (g)/4.5 g
1.	Anastrozole	0.3
2.	Poly(DL-lactide-co-glycolide) 50/50	1.2
3.	N, N Dimethyl Acetamide (DMA)	3

Procedure:

i) Anastrazole was weighed and dissolved in the required amount of DMA.

ii) Poly (DL-lactide-co-glycolide) (50/50) was added in the solution of step (i) after dissolving anastrazole in DMA

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Example-3: Anastrozole depot injection

S. No.	Ingredient	Quantity (g)/5.7 g
1.	Anastrozole	0.3
2.	Poly (DL-lactide-co-glycolide) 50/50	3
3.	N, N Dimethyl Acetamide (DMA)	2.4

Procedure:

i) Anastrazole was weighed and dissolved in the required amount of DMA.

ii) Poly (DL-lactide-co-glycolide) (50/50) was added in the solution of step (i) after dissolving anastrazole in DMA

iii) The component of step (ii) was kept at 2-8°C for overnight

iv) The component of step (iii) was checked for any undissolved particles.

Dissolution profile

S.No.	Time (Days)	% cumulative drug released **Parameters:** USP Apparatus I, 50 rpm, temp. 37°C, pH 7.4 Phosphate Buffer, Volume 1000 ml, Replacement with 10 ml of media
1.	0.042	2.4
2.	0.17	2.9
3.	0.33	5.9
4.	0.5	4.8
5.	1	5.6
6.	2	6.5
7.	5	22.2
8.	6	26.5
9.	7	31.2
10.	10	40.8
11.	15	39.4
12.	20	43.3
13.	25	64.5
14.	30	81.5
15.	35	92.9

Example 4: Letrozole depot injection

S. No.	Ingredient	Quantity (mg)/600 mg
1.	Letrozole	75
2.	Poly(DL-lactide-co-glycolide) 75//25 (high viscosity)	150
3.	N, N Dimethyl Acetamide (DMA)	375

Procedure:

i) Letrazole was weighed and dissolved in the DMA.

ii) Poly (DL-lactide-co-glycolide) 75//25 (high viscosity) was added in the solution of step (i) after dissolving Letrazole in DMA.

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Example 5: Letrozole depot injection

S. No.	Ingredient	Quantity(mg)/600 mg
1.	Letrozole	75
2.	Poly(DL-lactide-co-glycolide) 75//25 (high viscosity)	125
3.	N,N-Dimethyl Acetamide (DMA)	200
4.	Dimethyl Isosorbide (DMI)	200

Procedure:

i) Letrazole was weighed and dissolved in the mixture of DMA and DMI.

ii) Poly (DL-lactide-co-glycolide) 75//25 (high viscosity) was added in the solution of step (i) after dissolving Letrazole in DMA and DMI.

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Example 6: Letrozole depot injection

S. No.	Ingredient	Quantity(mg)/700 mg
1.	Letrozole	75
2.	Poly(DL-lactide-co-glycolide) 50/50 (low viscosity)	225
3.	N, N-Dimethyl Acetamide (DMA)	400

Procedure:

i) Letrazole was weighed and dissolved in the DMA.

ii) Poly (DL-lactide-co-glycolide) 50/50 (low viscosity) was added in the solution of step (i) after dissolving Letrazole in DMA.

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Example 7: Letrozole depot injection

S. No.	Ingredient	Quantity(mg)/550 mg
1.	Letrozole	75
2.	Poly(DL-lactide-co-glycolide) 50/50 (low viscosity)	125
3.	N, N-Dimethyl Acetamide (DMA)	350

Procedure:

i) Letrazole was weighed and dissolved in the DMA.

ii) Poly (DL-lactide-co-glycolide) 50/50 (low viscosity) was added in the solution of step (i) after dissolving Letrazole in DMA.

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Example 8: Tamsulosin depot injection

S. No.	Ingredient	Quantity (g)/unit dose
1.	Tamsulosin Hydrochloride	0.127
2.	Poly(DL-lactide-co-glycolide) 50/50	0.874
3.	N,N Dimethyl Acetamide (DMA)	6

Procedure:

i) Tamsulosin was weighed and dissolved in the DMA.

ii) Poly (DL-lactide-co-glycolide) 50/50 was added in the solution of step (i) after dissolving Tamsulosin in DMA.

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Dissolution profile

S.No.	Time (Days)	% Mean drug released **Parameters:** USP Apparatus I, 50 rpm, temp. 37°C, Phosphate Buffer pH 7.4, Volume 900 ml, Replacement with 2 ml of media
1.	0.16	83.45
2.	1	92.95
3.	2	76.85
4.	4	82.75
5.	7	76.7
6.	11	85.1

Example 9: Tamsulosin depot injection

S. No.	Ingredient	Quantity (g)/unit dose
1.	Tamsulosin base	0.096
2.	Poly(DL-lactide-co-glycolide) 50/50	1.92
3.	N,N-Dimethyl Acetamide (DMA)	1.46

Procedure:

i) Tamsulosin was weighed and dissolved in the DMA.

ii) Poly (DL-lactide-co-glycolide) 50/50 was added in the solution of step (i) after dissolving Tamsulosin in DMA.

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Dissolution profile

S.No.	Time (Days)	% Mean drug released **Parameters:** USP Apparatus II, 50 rpm, temp. 37°C, Phosphate Buffer pH 7.4, Volume 1000 ml, Replacement with 5 ml of media
1.	0.17	0.7
2.	1	4.2
3.	3	6.2

4.	6	27.1
5.	10	49.0
6.	29	96.1
7.	37	108.3

Example 10: Donepezil depot injection

S. No. Ingredient	Quantity(mg)/unit dose
1. Donepezil base	90
2. Poly (DL-lactide-co-glycolide) 75/25	360
3. N,N-Dimethyl Acetamide (DMA)	450

Procedure:

i) Dozepezil was weighed and dissolved in the DMA.

ii) Poly (DL-lactide-co-glycolide) 75/25 was added in the solution of step (i) after dissolving Dozepezil in DMA.

iii) The component of step (ii) was kept at 2-8°C for overnight.

iv) The component of step (iii) was checked for any undissolved particles.

Dissolution profile

S.No.	Time (Days)	% Mean drug released **Parameters:** USP Apparatus II, 50 rpm, temp. 37°C, pH 7.4 Phosphate Saline Buffer Solution, Volume 1000 ml, sampling volume 1.5 ml
1.	0	0
2.	0.33	7.1
3.	1	12.9
4.	3	15.7
5.	7	16.4
6.	10	22.5
7.	15	36.5
8.	20	63.3
9.	27	94.6

Example-11: Letrozole depot injection

S. No.	Ingredient	Quantity/unit dose (mg)
1.	Letrozole	150
2.	Poly(lactide-co-glycolide) co-polymer	400
3.	N-methyl-2-pyrrolidone	2

Procedure:

i) Poly(lactide-co-glycolide) co-polymer was dissolved in N-methyl-2-pyrrolidone and suitably filled in an ampoule.

ii) Letrozole was lyophilized and filled in a suitable vial.

iii) Step (i) solution of Poly(lactide-co-glycolide) co-polymer is added to step (ii) Letrozole powder and shaken well before administration.

Example-12: Tamsulosin depot injection

S. No.	Ingredient	Quantity/unit dose (mg)
1.	Tamsulosin	12
2.	Poly (lactide-co-glycolide) co-polymer	240
3.	N-methyl-2-pyrrolidone	0.5

Procedure:

i) Sterile Tamsulosin and Poly(lactide-co-glycolide) co-polymer were mixed together.

ii) The material of step (i) and N-methyl-2-pyrrolidone were filled in separate chambers of pre-filled syringe.

iii) The materials of the syringe are mixed together before administration.

Example-13: Ziprasidone depot injection

S. No.	Ingredient	Quantity/unit dose (mg)
1.	Ziprasidone	150
2.	Poly(lactide-co-glycolide)	240
3.	N-methyl-2-pyrrolidone	2

Procedure:

i) Poly(lactide-co-glycolide) is dissolved in N-methyl-2-pyrrolidone.

ii) The solution is filtered through 0.2 micron and suitably filled in vial or ampoule.

iii) Ziprasidone is filled in a suitable vial followed by sterilization of the same.

iv) Step (ii) solution of Poly(lactide-co-glycolide) is added to step (iii) Ziprasidone powder and shaken well to obtain a uniform dispersion suitable for parenteral administration.

Example-14: Olanzapine depot injection

S. No.	Ingredient	Quantity/unit dose (mg)
1.	Olanzapine	80
2.	Poly(lactic acid)	250
3.	N-methyl-2-pyrrolidone	1

Procedure:

i) Poly (lactic acid) is dissolved in N-methyl-2-pyrrolidone.

ii) The solution is filtered through 0.2 micron and suitably filled in vial or ampoule.

iii) Sterile Olanzapine is filled in a suitable vial.

iv) Step (ii) solution of Poly (lactic acid) is added to step (iii) Olanzapine powder and shaken well to obtain a uniform dispersion suitable for parenteral administration.

Example-15: Aripiprazole depot injection

S. No.	Ingredient	Quantity/unit dose (mg)
1.	Aripiprazole	100
2.	Poly (lactic acid)	100
3.	N-methyl-2-pyrrolidone	1

Procedure:

i) Sterile Aripiprazole and Poly (lactic acid) are mixed together.

ii) The material of step (i) and N-methyl-2-pyrrolidone are filled in separate chambers of pre-filled syringe.

iii) The materials of the syringe are mixed together before administration.

Example-16: Anastrazole depot injection

S. No.	Ingredient	Quantity/unit dose (mg)
1.	Anastrozole	30
2.	Poly(Sebacic acid: Ricinoleic acid)	240
3.	N-methyl-2-pyrrolidone	0.3

Procedure:

i) Poly(Sebacic acid: Ricinoleic acid) is dissolved in N-methyl-2-pyrrolidone and suitably filled in an ampoule.

ii) Sterile Anastrozole is filled in a suitable vial.

iii) Step (i) solution of Poly(Sebacic acid: Ricinoleic acid) is added to step (ii) Anastrozole powder and shaken well to reconstitute before administration.

Example-17: Anastrazole depot injection

S. No.	Ingredient	Quantity/unit dose (mg)
1.	Anastrozole	20
2.	Poly(Sebacic acid: Ricinoleic acid)	240
3.	N-methyl-2-pyrrolidone	1
4.	Dimethyl acetamide	0.2

Procedure:

i) Anastrozole is filled in a vial to form component-1.

ii) Poly (Sebacic acid: Ricinoleic acid) is dissolved in a mixture of N-methyl-2-pyrrolidone and Dimethyl acetamide to form component-2.

iii) The component-1 of step (i) is mixed with component-2 of step (ii) to obtain the desired composition before administration.

We claim:

1. An injectable composition comprising at least one active agent(s) selected from a group comprising antipsychotics, aromatase inhibitors, alpha-1 adrenergic blocking agents, acetylcholinesterase inhibitors and their pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s) wherein the said compositions provide a prolonged release of the active agent(s) for extended periods of time.

2. A composition according to claim 1, wherein the composition comprises as the active agent at least one antipsychotic preferably ziprasidone or olanzapine or aripiprazole, or at least one aromatase inhibitor preferably anastrozole or letrozole, or at least one adrenergic blocking agent preferably tamsulosin, or at least one acetylcholinesterase inhibitor preferably donepezil; or pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein these are in the form of an in situ gelling composition or an implant composition and which form a depot upon administration in vivo upon contact with body fluids therefore providing a prolonged release of the active agent for extended periods of time.

3. A composition according to claim 1 or 2, wherein the composition is a single-component or a multi-component injectable depot composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof from about 0.1% w/w to about 95% w/w; at least one biocompatible bioerodible

polymer(s) in an amount of from about 0.1% w/w to about 95% w/w; at least one biocompatible non-toxic solvent(s) in an amount of from about 0.1% w/w to about 95% w/w and one or more pharmaceutically acceptable excipient(s) in an amount of from about 0% to about 99.8% w/w based upon the total weight of the composition, such that the said composition is in the form of ready-to-use liquid solution or dispersion, or a reconstitutable composition, and such that the said composition provides a prolonged release of the active agent(s) for extended periods of time.

4. A composition of according to claim 3, wherein the composition is single-component composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more excipient(s), wherein the said composition is in the form of ready-to-use liquid solution or dispersion.

5. A composition according to claim 3, wherein the composition is a multi-component composition comprising of at least two components component-1 and component-2 such that the said composition is in the form of a reconstitutable composition, wherein component-1 comprises at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof, optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein component-2 for reconstitution of component-1 comprises at least one biocompatible non-toxic solvent(s), optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s).

6. The composition according to any of the preceding claims 1 to 5, wherein the biocompatible bioerodible polymer(s) is a lactic or glycolic acid based polymer.

7. A composition according to claim 6, wherein the lactic or glycolic acid based polymer is polylactide polymer (PLA), or a polyglycolide polymer, or a poly (lactide-co-glycolide) co-polymer (PLGA).

8. The composition according to any one of the preceding claims 1 to 7, wherein the composition provides in situ gelling composition comprising the active agent and preferably a PLGA polymer, dissolved or dispersed or suspended in suitable solvent optionally further dissolved or dispersed or suspended in a liquid diluent such as an aqueous vehicle or an organic solvent or an oily vehicle.

9. A composition according to claim 3, wherein the composition is the single-component or a multi-component injectable depot composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more pharmaceutically acceptable excipient(s), wherein the said biocompatible non-toxic solvent(s) is capable of dissolving or dispersing the active agent and the biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein upon administration in vivo the composition is capable of precipitating to form a substantially cohesive gel or implant almost instantaneously.

10. The composition according to any one of the preceding claims 1 to 9, wherein the compositions provide a flowable composition for forming a solid or semi-solid biodegradable gel or implant in situ within a living body comprising ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil as active agent, at least one biocompatible bioerodible polymer(s) and at least one biocompatible non-toxic solvent(s), optionally at least one gelling

agent(s) and optionally along with one or more pharmaceutically acceptable excipient(s), wherein the composition upon in vivo administration exhibits minimal burst effect thus avoiding dose dumping and providing a sustained release of the active agent for a prolonged duration.

11. A composition according to claim 3, wherein the composition is a single-component or a multi-component injectable depot composition comprising at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s) and optionally one or more pharmaceutically acceptable excipient(s), wherein the composition additionally comprises at least one gelling agent(s) preferably in an unhydrated form.

12. The composition according to any one of the claims 1 to 11, wherein the composition comprises at least one active agent selected from a group comprising ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s) in the form of a multi-component system preferably comprising at least two components.

13. A composition according to claim 12, wherein the composition is a two-component composition comprising of component-1 and component-2 such that the said composition is in the form of a reconstitutable composition, wherein component-1 comprises at least one active agent(s) selected from a group consisting of ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil, and pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof, optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s);

and wherein component-2 for reconstitution of component-1 comprises at least one biocompatible non-toxic solvent(s), optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); and wherein the composition optionally comprise at least one gelling agent(s) either present in component-1 or component-2 or both.

14. The composition according to any one of the claims 1 to 13, wherein the gelling agent(s) is a biocompatible cellulosic polymer which acts as a stabilizer, active agent release modifier and/or a gel forming agent.

15. A composition according to claim 14, wherein the gelling agent is selected from but not limited to group comprising cellulose derivatives, such as hydroxypropyl cellulose, hydroxyethyl cellulose, hydroxypropyl methyl cellulose, methylcellulose, sodium carboxymethyl cellulose and its derivatives, vinyl polymers, polyoxyethylene-polyoxypropylene polymers or co-polymers (Pluronics®), such as PEO_{99}-PPO_{67}-PEO_{99} known as Pluronics F127, polysaccharides such as glycosaminoglycans, agar, pectin, alginic acid, sodium alginate, dextran, starch and chitosan, proteins, poly(ethyleneoxide), acrylamide polymers, polyhydroxy acids, polyanhydrides, polyorthoesters, polyamides, polycarbonates, polyalkylenes, polyalkylene glycols, polyalkylene oxides, polyalkylene terepthalates, polyvinyl alcohols such as polyacrylic acid, polymethacrylic acid, polyvinyl pyrrolidone and polyvinyl alcohol, polyvinyl ethers, polyvinyl esters, polyvinyl halides, polyvinylpyrrolidone, polysiloxanes, polyvinyl acetates, polystyrene, polyurethanes, synthetic celluloses, polyacrylic acids, polybutyric acid, polyvaleric acid, poly(lactide-co-caprolactone), and copolymers, derivatives, and the like; or mixtures thereof.

16. A composition according to claim 15, wherein the gelling agent is present in an amount between about 0.1 to about 50%, more preferably between about 0.5 to about 50% by weight of either component-1 or component-2 or both.

17. The composition according to any one of the claims 1 to 16, wherein the injectable compositions comprising at least one active agent selected from a group

comprising ziprasidone, olanzapine, aripiprazole, anastrozole, letrozole, tamsulosin and donepezil; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the said biocompatible non-toxic solvent(s) is capable of dissolving or dispersing the active agent and/or the biocompatible bioerodible polymer(s); and wherein upon administration in vivo the composition is capable of precipitating to form a substantially cohesive gel or implant almost instantaneously.

18. The composition according to any one of the claims 1 to 17, wherein the biocompatible bioerodible polymer is selected from a group comprising lactic acid-based polymers such as polylactides e.g. poly (D,L-lactide) i.e. PLA; glycolic acid-based polymers such as polyglycolides (PGA) e.g. Lactel® from Durect; poly (D,L-lactide-co-glycolide) i.e. PLGA, (Resomer® RG-504, Resomer® RG-502, Resomer® RG-504H, Resomer® RG-502H, Resomer® RG-504S, Resomer® RG-502S, from Boehringer, Lactel® from Durect); polycaprolactones such as Poly(e-caprolactone) i.e. PCL (Lactel® from Durect); polyanhydrides; poly(Sebacic acid) SA; poly(Ricenolic acid) RA; poly(Fumaric acid), FA; poly(Fatty acid dimmer), FAD; poly(terephthalic acid), TA; poly(isophthalic acid), IPA; poly(p-{carboxyphenoxy}methane), CPM; poly(p-{carboxyphenoxy}propane), CPP; poly(p-{carboxyphenoxy}hexane), CPH; polyamines, polyurethanes, polyesteramides, polyorthoesters {CHDM: Cis/trans-cyclohexyl dimethanol, HD:1,6-hexanediol. DETOU: (3,9-diethylidene-2,4,8,10-tetraoxaspiro undecane)}; polydioxanones; polyhydroxybutyrates; polyalkyene oxalates; polyamides; polyesteramides; polyurethanes; polyacetals; polyketals; polycarbonates; polyorthocarbonates; polysiloxanes; polyphosphazenes; succinates; hyaluronic acid; poly(malic acid); poly(amino acids); polyhydroxyvalerates; polyalkylene succinates; polyvinylpyrrolidone; polystyrene; synthetic celluloses; polyacrylic acids; polybutyric acid; triblock copolymers (PLGA-PEG-PLGA), triblock copolymers (PEG-PLGA-PEG), poly (N-isopropylacrylamide) (PNIPAAm), poly (ethylene oxide)- poly (propylene oxide)- poly (ethylene oxide) tri-block copolymers (PEO-PPO-PEO), polyvaleric acid; polyethylene glycol; polyhydroxycellulose; chitin; chitosan; polyorthoesters

and copolymers, terpolymers; lipids such as cholesterol, lecithin; poly(glutamic acid-co-ethyl glutamate) and the like, or mixtures thereof.

19. A composition according to claim 18, wherein the biodegradable polymer is a lactic acid-based polymer, more preferably polylactide, or poly (D, L-lactide-co-glycolide) i.e. PLGA.

20. A composition according to claim 19, wherein the biodegradable polymer is present in an amount between about 10% to about 98% w/w of the component-1.

21. A composition according to claim 19, wherein the lactic acid-based polymer has a monomer ratio of lactic acid to glycolic acid in the range of 100:0 to about 0:100 preferably 100:0 to about 10:90.

22. The composition according to any one of the claims 1 to 21, wherein the biocompatible non-toxic solvent is selected from a group comprising triacetin, ethanol, bezyl alcohol, 1-butanol, 2-butanol, chloroform, acetic acid, isopropyl alcohol, acetonitrile, N-methyl-2-pyrrolidone (NMP), 2-pyrrolidone, miglyol, glycerol, methyl acetate, methyl isobutyl ketone, benzyl benzoate, propylene glycol, dimethyl isosorbide, propylene carbonate, ethyl acetate, ethyl lactate, dimethyl sulfone, N,N-diethyl-m-toluamide, methyl ethyl ketone, dimethylformamide, dichloromethane, benzonitrile, dimethyl isosorbide, dimethyl sulfoxide, dimethylacetamide, tetrahydrofuran, caprolactam, decymethylsulfoxide, oleic acid, and 1-dodecylazacyclo-heptan-2-one, and the like or mixtures thereof.

23. The composition according to claim 1, comprising ziprasidone; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more excipient(s), wherein the solvent is selected from a group comprising N-methyl-2-pyrrolidone, dimethyl sulfoxide (DMSO), dimethyl formamide (DMF), methyl isobutyl ketone, or mixtures thereof.

24. The composition according to claim 1, comprising olanzapine; at least one

biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

25. The composition according to claim 1, comprising aripiprazole; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

26. The composition according to claim 1, comprising anastrozole; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

27. The composition according to claim 1, comprising letrozole; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

28. The composition according to claim 1, comprising tamsulosin; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

29. The composition according to claim 1, comprising donepezil; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), wherein the solvent is selected from a group comprising ethylacetate, N-methyl-2-pyrrolidone, dimethylformamide, dimethyl sulfoxide, dimethyl acetamide, 1-butanol, 2-butanol, or mixtures thereof.

30. The composition according to claims 1 to 29, wherein the injectable compositions comprises as the active agent at least one antipsychotic preferably ziprasidone or olanzapine or aripiprazole, or at least one aromatase inhibitor preferably anastrozole or letrozole, or at least one adrenergic blocking agent preferably tamsulosin, or at least one acetylcholinesterase inhibitor preferably donepezil, or pharmaceutically acceptable salts, derivatives, isomers, polymorphs, solvates, hydrates, analogues, enantiomers, tautomeric forms or mixtures thereof; at least one biocompatible bioerodible polymer(s); at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s), is further diluted with an aqueous, hydro-alcoholic or oily liquid vehicle prior to parenteral administration.

31. A composition according to claim 30, wherein the liquid vehicle is in the form of an aqueous vehicle comprising water and optionally water miscible solvent selected from group comprising preferably a water-miscible alcohol, for example, ethanol, n-propyl alcohol, isopropyl alcohol, tert-butyl alcohol, ethylene glycol or propylene glycol; dimethylsulfoxide; decylmethylsulfoxide; dimethylformamide; N-methyl-2-pyrrolidone; 2-pyrrolidone; acetone; methyl acetate; ethyl acetate; caprolactam; oleic acid, and 1-dodecylazacycloheptan-2-one; a water-miscible ether, for example tetrahydrofuran; a water-miscible nitrile, for example acetonitrile; a water-miscible ketone, for example acetone or methyl ethyl ketone; an amide, for example dimethylacetamide; propylene glycol; glycerin, polyethylene glycol 400, glycofurol (tetraglycol), purified water and the like; or mixtures thereof.

32. The composition according to any one of the preceding claims 1 to 31, wherein the solvent is selected from preferably a group comprising glycerin, ethanol, propylene glycol, polyethylene glycols, NMP, and purified water.

33. A composition according to claim 30, wherein the liquid diluent is a lipophilic or oily vehicle comprising at least one oily component selected from a group comprising vegetable oils such as corn oil, sesame oil, coconut oil, almond oil, sunflower oil, castor oil, etc. or a lipophilic compound such as dimethyl isosorbide, optionally with a surfactant selected from a group comprising anionic, cationic, non-ionic or zwitterionic surfactants and/or one or more other pharmaceutically acceptable excipient(s).

34. The composition according to any one of the preceding claims 1 to 33, wherein the injectable depot compositions of the present invention comprise one or more pharmaceutically acceptable excipient(s) selected from a group comprising one or more co-surfactants, solvents/co-solvents, water immiscible solvents, water, water miscible solvents, oily components, hydrophilic solvents, emulsifiers, preservatives, antioxidants, anti-foaming agents, stabilizers, buffering agents, pH adjusting agents, osmotic agents, channel forming agents, isotonicity producing agents, or any other excipient known to the art that is soluble or miscible or dispersible in the biocompatible non-toxic solvent(s), or mixtures thereof.

35. A composition according to claim 34, wherein the co-surfactant is selected from a group comprising polyethylene glycols; polyoxyethylene-polyoxypropylene block copolymers known as "poloxamer"; polyglycerin fatty acid esters such as decaglyceryl monolaurate and decaglyceryl monomyristate; sorbitan fatty acid ester such as sorbitan monostearate; polyoxyethylene sorbitan fatty acid ester such as polyoxyethylene sorbitan monooleate(TWEEN®); polyethylene glycol fatty acid ester such as polyoxyethylene monostearate; polyoxyethylene alkyl ether such as polyoxyethylene lauryl ether; polyoxyethylene castor oil and hardened castor oil, such as polyoxyethylene hardened castor oil; and the like or mixtures thereof; the solvent/cosolvent is selected from but not limited to a group comprising alcohols such as propylene glycol, polypropylene glycol, polyethylene

glycol (such as PEG300, 400, 600, etc.), glycerol, ethanol, triacetin, dimethyl isosorbide, glycofurol, propylene carbonate, water, dimethyl acetamide, and the like or mixtures thereof; anti-foaming agents include for example silicon emulsions or sorbitan sesquioleate; suitable stabilizers to prevent or reduce the deterioration of the other components in compositions of the present invention include antioxidants such as glycine, alpha-tocopherol or ascorbate, BHA, BHT, and the like or mixtures thereof; suitable tonicity modifier includes for example mannitol, sodium chloride, and glucose; suitable buffering agent includes for example acetates, phosphates, and citrates with suitable cations.

36. A pharmaceutical kit suitable for in situ formation of a biodegradable depot gel or implant from the compositions according to claim 1, in the body of a subject in need thereof, which comprises a device containing ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil as active agent, optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutical acceptable excipient(s); and a device containing at least one biocompatible non-toxic solvent(s), optionally at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s); wherein the devices allow for expulsion of the contents of the two devices for enabling mixing together prior to administration of the contents into the body of the subject in need thereof.

37. The composition according to any one of the preceding claims 1 to 36, wherein the composition comprises additionally a thermogelling or hydrogelling polymer, or the biocompatible bioerodible polymer is a temperature sensitive biocompatible polymer, for example, a block copolymer having thermal gelation properties wherein the polymer is a gel at physiological temperatures (about 37°C) and is a liquid above or below physiological temperatures would be functional.

38. A composition according to any one of the preceding claims 1 to 37, wherein the viscosity of the injectable composition is from about 1 cps to about 5000 cps or from about 1 cps to about 3000 cps or from about 1 cps to about 800 cps.

39. A process for preparation of such injectable compositions according to any one of the preceding claims 1 to 36, which comprises mixing together the active agent(s), at least one biocompatible bioerodible polymer(s), at least one biocompatible non-toxic solvent(s), and optionally one or more pharmaceutically acceptable excipient(s) to form a single-component ready-to-use liquid solution or dispersion; or preparing a multi-component reconstitutable composition which comprises preparation of component-1 using the active agent(s) alone or mixing the active agent(s) together with at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s), and preparation of component-2 using at least one biocompatible non-toxic solvent(s) alone or a dispersion thereof comprising at least one biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s) dispersed in the biocompatible non-toxic solvent(s), and reconstituting the component-1 using the component-2 prior to administration.

40. A process for the preparation of injectable composition according to any one of the preceding claims 1 to 36, which comprises of the following steps:
   i) Dissolving or dispersing the active agent, biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s) in a biocompatible non-toxic solvent(s) and
   ii) Filling the material of step (i) into a syringe suitable for parenteral administration.

41. A process for the preparation of injectable composition according to any one of the preceding claims 1 to 36, which comprises of the following steps:
   i) Dissolving or dispersing the biocompatible bioerodible polymer(s) and optionally one or more pharmaceutically acceptable excipient(s) in a biocompatible non-toxic solvent(s),
   ii) Lyophilizing and filling the active agent(s) optionally mixed with one or more pharmaceutically acceptable excipient(s) in a vial, and
   iii) Reconstituting the material of step (ii) with the material of step (i) before administration.

42. A process for the preparation of injectable composition according to any one of the preceding claims 1 to 36, which comprises of the following steps:
    i) Mixing the sterile active agent(s), biocompatible bioerodible polymer(s) and optionally one or more excipient(s),
    ii) Filling the material of step (i) and the biocompatible non-toxic solvent(s) optionally comprising one or more pharmaceutically acceptable excipient(s) in separate chambers of pre-filled syringe, and
    iii) Mixing the materials of the pre-filled syringe before administration.

43. A process for the preparation of injectable composition according to any one of the preceding claims 1 to 36, which comprises of the following steps:
    i) Mixing the sterile active agent(s), biocompatible bioerodible polymer(s) and optionally one or more excipient(s),
    ii) Filling the material of step (i) in a syringe,
    iii) Filling the biocompatible non-toxic solvent(s) optionally comprising one or more pharmaceutically acceptable excipient(s) in a suitable container, and
    iv) Reconstituting the material of step (ii) using the material of step (iii) before administration.

44. A process for preparation of such composition to any one of the preceding claims 1 to 36, which comprises of the following steps:
    i) Dissolving or dispersing the active agent(s), biocompatible bioerodible polymer(s) and optionally one or more excipient(s) in biocompatible non-toxic solvent(s),
    ii) Optionally making a liquid diluent composition (vehicle) comprising mixing a water miscible or immiscible solvent or an oily compound optionally with gelling agent(s) and/or other excipient(s), and
    iii) Optionally reconstituting the material of step (i) with the material of step (ii) before administration.

45. A process for preparation of such composition according to any one of the preceding claims 1 to 36, which comprises of the following steps:
    i) Mixing the sterile active agent(s) with biocompatible bioerodible polymer(s),

ii) Mixing the material of step (i) optionally with gelling agent and/or optionally with one or more excipient(s),

iii) Dispersing material of step (ii) in a biocompatible non-toxic solvent(s) to form component-1,

iv) Mixing the liquid diluent (vehicle) optionally with gelling agent(s) and/or other excipient(s) to form component- 2, and

v) Mixing the component-1 and component-2 to obtain the desired composition before administration.

46. The composition according to any one of the preceding claims 1 to 45, wherein the composition is preferably in the form of parenteral composition which can be administered to a subject, animals or humans, preferably via intramuscular, intradermal, cutaneous or subcutaneous routes.

47. A method of forming a depot gel or an implant in situ, in a living body according to claim 1, which comprises preparing an in situ gelling formulation according to the method described herein, placing the formulation within the body and allowing the liquid vehicle to disperse or dissipate to produce a solid or gel implant.

48. Use of an in situ gelling formulation according to claim 1 in the manufacture of a medicament for the treatment of a condition treatable by ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil in a mammal particularly a human being.

49. A method of using the compositions of ziprasidone or olanzapine or aripiprazole or anastrozole or letrozole or tamsulosin or donepezil according to claim 1, which comprises administering to a subject/patient in need thereof an effective amount of the said composition.

50. A method according to claim 49, comprising ziprasidone particularly useful for management such as prophylaxis, amelioration and/or treatment of subjects for the signs and symptoms of schizophrenia; comprising olanzapine particularly

useful for management such as prophylaxis, amelioration and/or treatment of schizophrenia, acute manic episodes in bipolar disorder, acute agitation associated with both these disorders, maintenance treatment in bipolar disorder and depressive episodes associated with bipolar disorder; comprising aripiprazole particularly useful for management such as prophylaxis, amelioration and/or treatment of schizophrenia; compositions comprising anastrozole are particularly useful for management such as prophylaxis, amelioration and/or treatment of postmenopausal women with hormone receptor positive early breast cancer; comprising letrozole particularly useful for the management such as prophylaxis, amelioration and/or treatment of hormonally-responsive breast cancer; compositions comprising tamsulosin are particularly useful for management such as prophylaxis, amelioration and/or treatment of subjects for the signs and symptoms of benign prostatic hyperplasia; and comprising donepezil particularly useful for the management such as prophylaxis, amelioration and/or treatment of mild to moderate Alzheimer's dementia and attention deficit disorder.

51. Use of the composition according to claim 1, comprising ziprasidone or olanzapine or aripiprazole as the active agent for the manufacture of a medicament for the prophylaxis, amelioration and/or treatment of signs and symptoms of schizophrenia.

52. The injectable compositions and process for the preparation of injectable compositions substantially as herein described and illustrated by the examples.

Figure 1

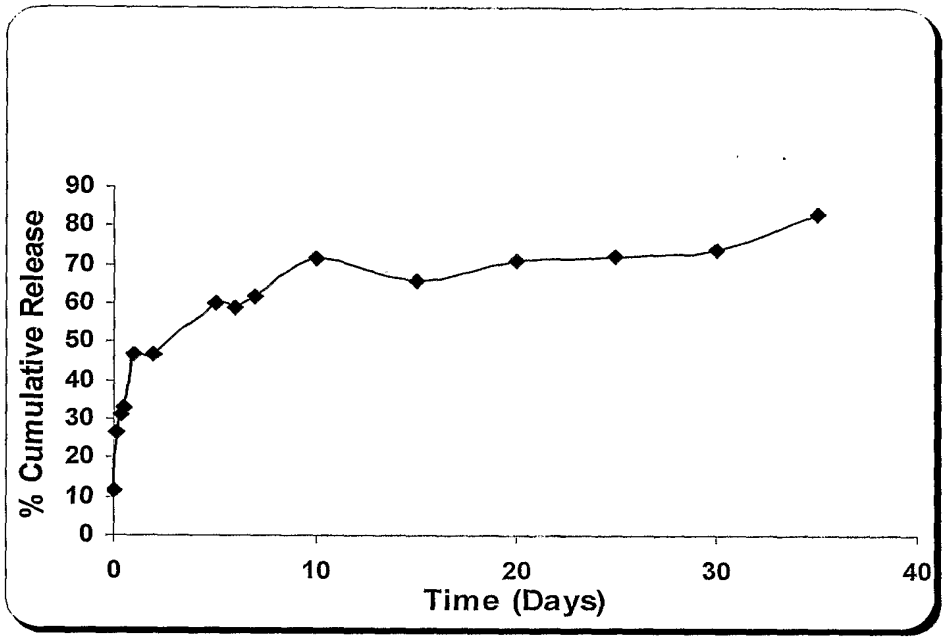

% Cumulative Release
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
Time (Days)

Figure 2

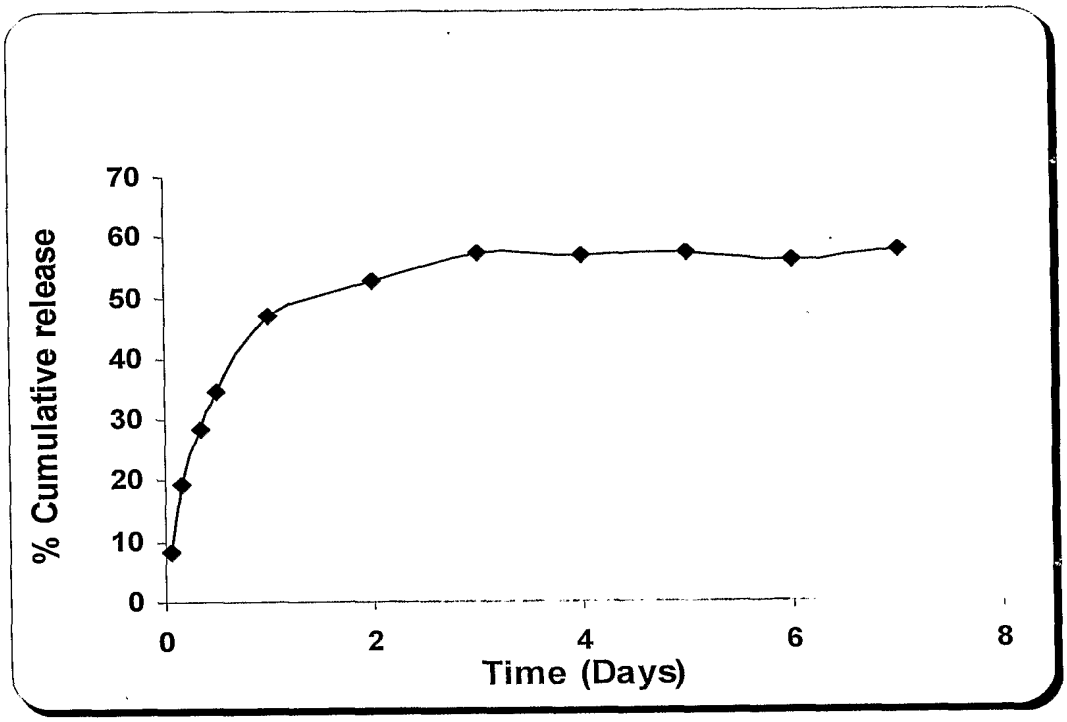


Figure 3

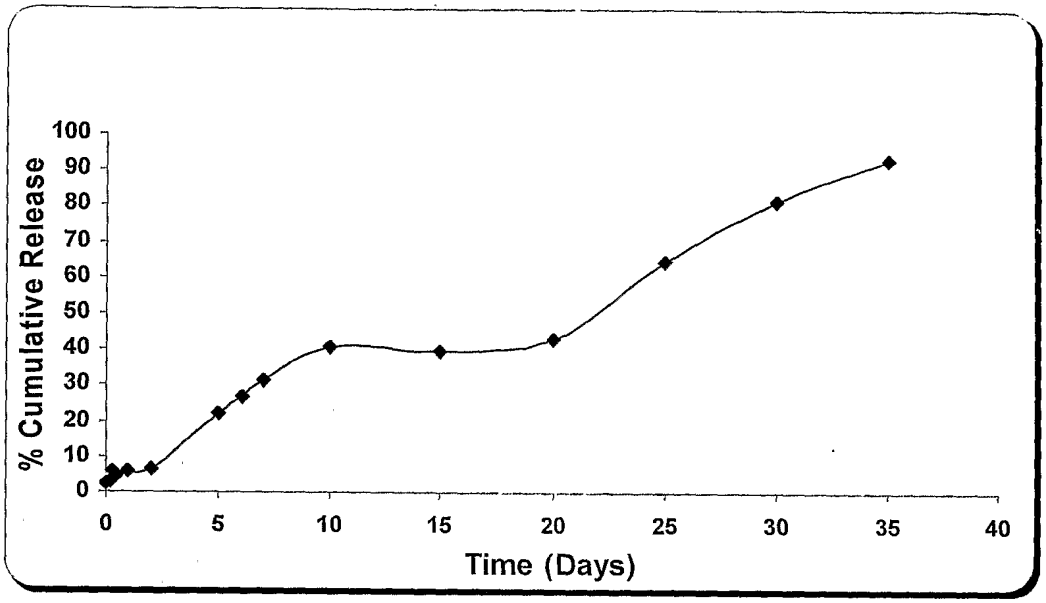

% Cumulative Release
100
90
80
70
60
50
40
30
20
10
0
0
5
10
15
20
25
30
35
40
Time (Days)

Figure 4

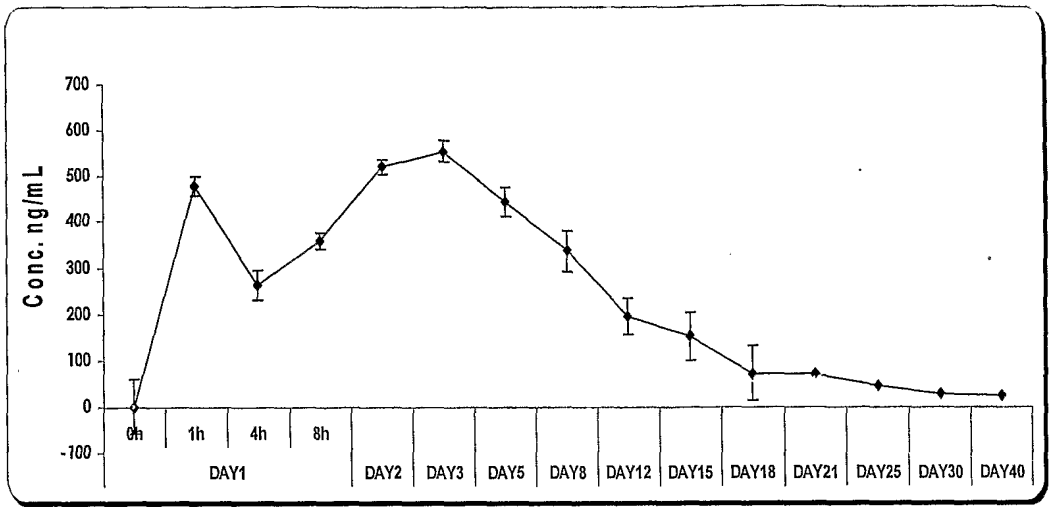

Conc. ng/mL
700
600
500
400
300
200
100
0
-100
0h
1h
4h
8h
DAY1
DAY2
DAY3
DAY5
DAY8
DAY12
DAY15
DAY18
DAY21
DAY25
DAY30
DAY40

Figure 5

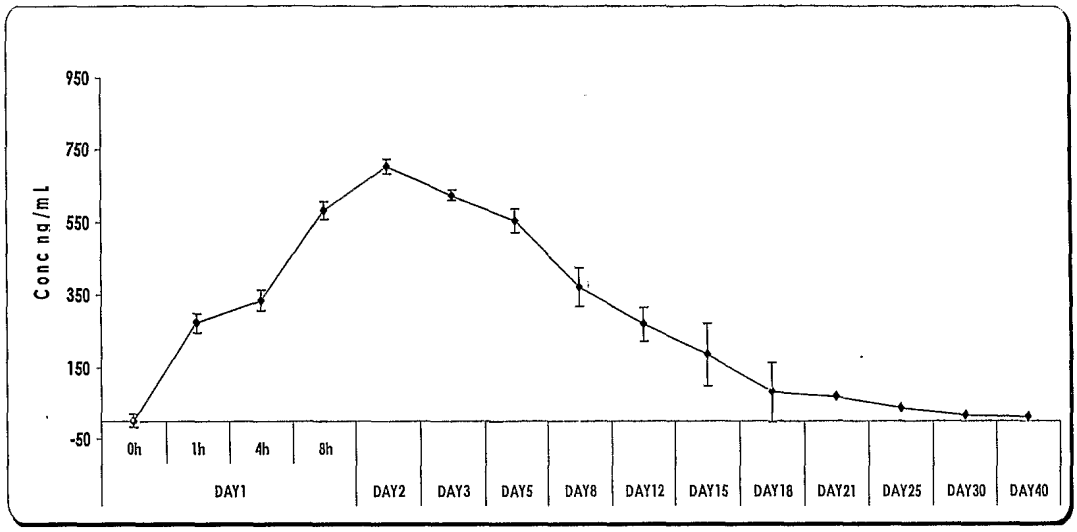

950
750
550
350
150
-50
Conc ng/ml
0h
1h
4h
8h
DAY1
DAY2
DAY3
DAY5
DAY8
DAY12
DAY15
DAY18
DAY21
DAY25
DAY30
DAY40

Figure 6

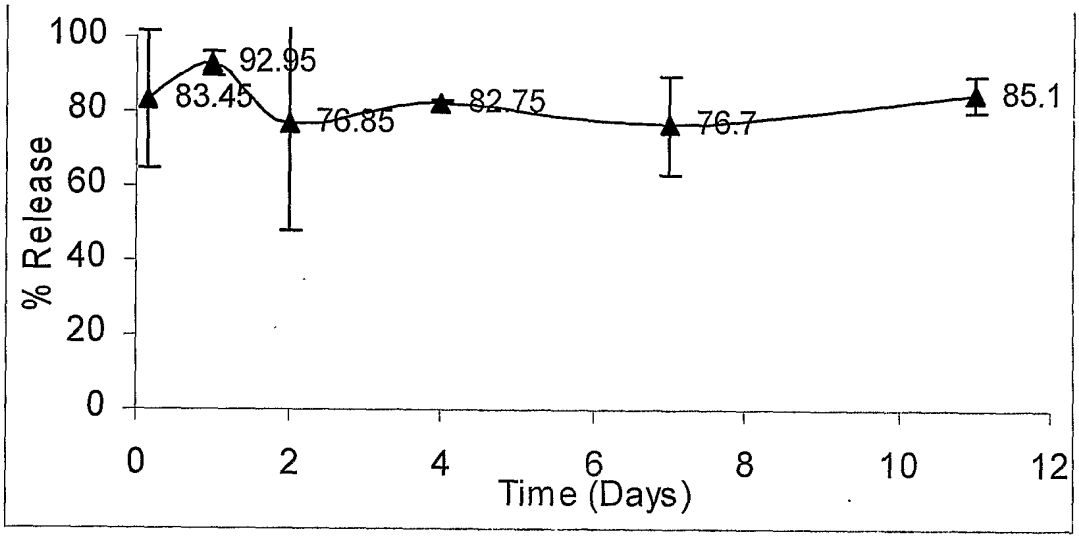

100
80
60
40
20
0
% Release
92.95
83.45
76.85
82.75
76.7
85.1
0
2
4
6
8
10
12
Time (Days)

Figure 7

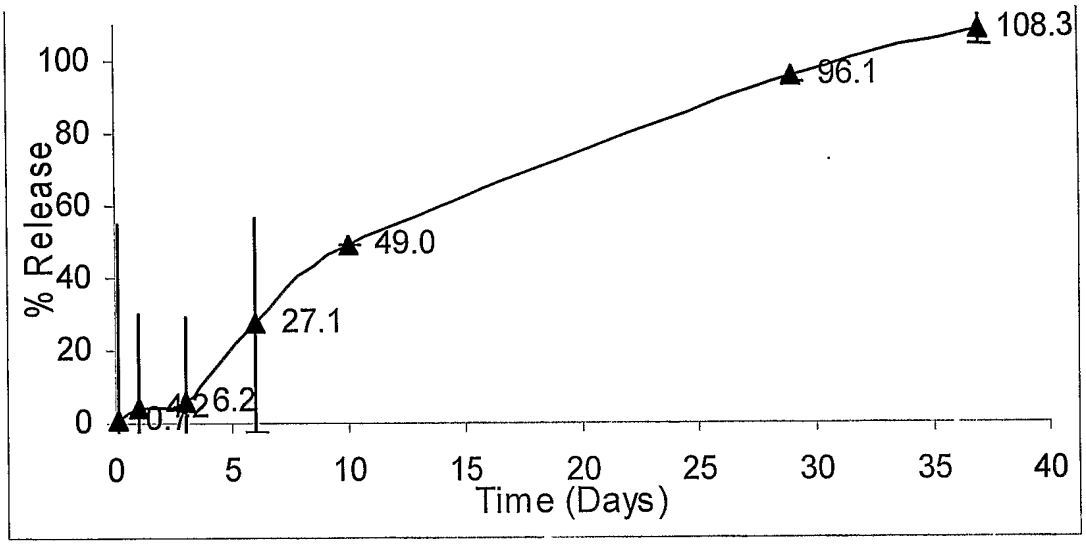

100
80
60
40
20
0
% Release
0
5
10
15
20
25
30
35
40
Time (Days)
108.3
96.1
49.0
27.1
6.2

Figure 8

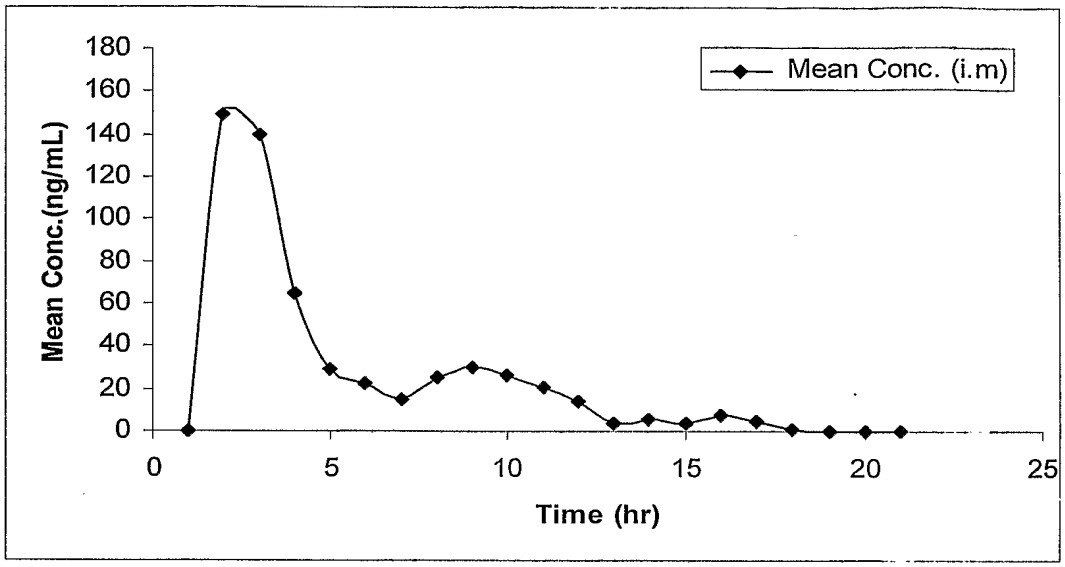
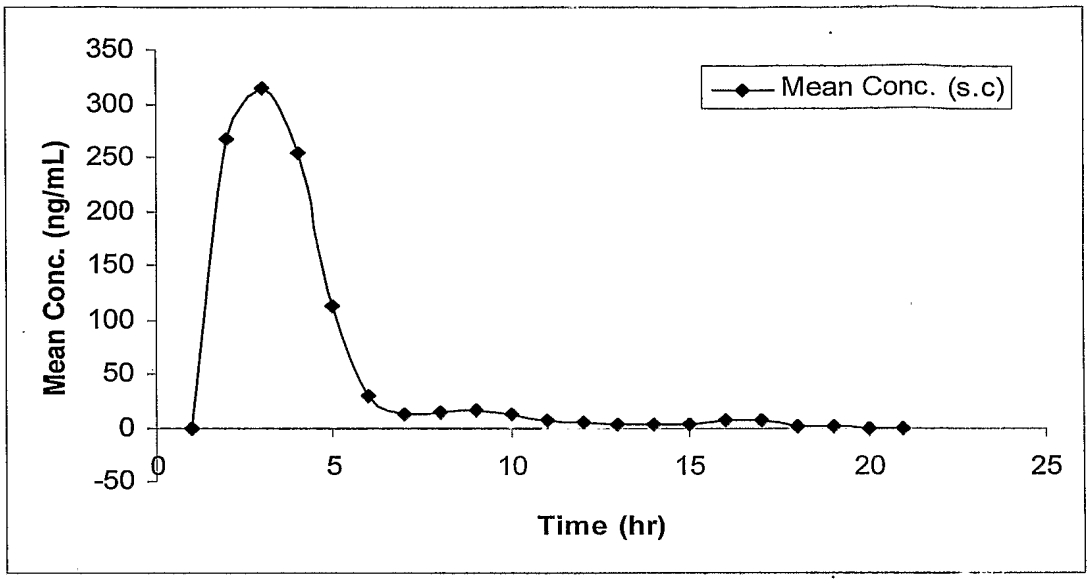

Mean Conc. (i.m)
Mean Conc.(ng/mL)
180
160
140
120
100
80
60
40
20
0
0
5
10
15
20
25
Time (hr)

Figure 9


Mean Conc. (s.c)
Mean Conc. (ng/mL)
350
300
250
200
150
100
50
0
-50
0
5
10
15
20
25
Time (hr)